13th International Symposium on HIV & Emerging Infectious Diseases

ISHEID

June 3-5, 2004

Toulon, FRANCE

"Palais Neptune"
International Convention Center

Final Program & Abstracts Book

International Symposium on HIV & Emerging Infectious Diseases

http://www.isheid.com

International HIV Persistence Workshop

http://www.hiv-workshop.com

CME on HIV & AIDS

http://www.hivaidsonline.com

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Chairman's Message

Dear Ladies, Gentlemen, Colleagues and Friends,
I am delighted to welcome you to this 13th edition of the "International Symposium on HIV & Emerging Infectious Diseases". Your enthusiasm for this event, witnessed by over 900 registrations from every continent and an ever-increasing number of excellent quality abstracts, is truly encouraging and has made the last two years of preparation worthwhile. I would also like to thank the Steering and Scientific Committees for their availability and the work they have accomplished, as well as the many industrial partners who have made this meeting possible.
Although AIDS no longer motivates public authorities as it did at the epidemic's onset, it remains a major public health issue as far as we - the people who fight it on a daily basis - are concerned. It is continuing to spread in Africa and Asia, despite repeated alerts from the field and the front stage currently occupied by global health issues; this urgent situation is further exacerbated by the fact that vaccine research is making little headway. In addition, the current evolution of health care in our so-called developed countries is cause for concern, and forces us to conclude that economic management is gradually shunting the values of knowledge and solidarity. Fundamental research has also paid the price of this dangerous ethos, whose field of vision is limited to the very short term. Just one "unforeseeable" health crisis is enough to reveal our health systems are overwhelmed and no longer equipped to respond. Nevertheless, in our role as scientists and in honor of the many patients we have lost, our mission is to ensure the values of knowledge and humanism triumph over the barbarism of our decision-makers. In this sense, the AIDS story will have proved a certain degree of activism must imperatively be maintained, and will constitute our only effective weapon in the face of the emerging infectious diseases set to challenge tomorrow's world.
I wish you a pleasant stay in Toulon and a fruitful meeting!

Alain Lafeuillade

Message du Président

Mesdames, Messieurs, chers collègues et amis,
C'est un grand plaisir pour moi de vous accueillir à cette 13e édition du "Symposium International sur le VIH & les Maladies Infectieuses Emergentes". Votre participation nombreuse, avec plus de 900 inscrits représentant toutes les zones géographiques de la planète, le nombre croissant -ainsi que la qualité- des abstracts reçus, constituent le plus bel encouragement qui soit et justifient les 2 années de préparation qui viennent de s'écouler. Je remercie également le Comité d'Organisation et le Comité Scientifique pour leur disponibilité, pour le travail effectué, ainsi que les nombreux partenaires industriels qui permettent à ce congrès d'avoir lieu.
Même si l'infection à VIH ne motive plus les pouvoirs publics comme au début de l'épidémie, elle reste pour nous qui la combattons au quotidien un problème majeur de santé publique. Son évolution continue en Afrique et Asie, malgré les alertes répétées du terrain, la place au premier plan des préoccupations de sécurité sanitaire à l'échelle de la planète ; et l'urgence est d'autant plus grande que la recherche vaccinale piétine. L'évolution de nos systèmes de santé en pays dits développés est préoccupante. Force est de constater que la gestion économique a peu à peu pris le pas sur les valeurs de connaissance et solidarité. La recherche fondamentale a également fait les frais de ce système de pensée dont le champ de vision se situe à très court terme. Il suffit d'une crise sanitaire "imprévisible" pour constater que nos systèmes de soins sont dépassés et n'ont plus les moyens d'y répondre.
Notre mission pourtant, en tant que scientifiques et en mémoire des nombreux malades que nous avons perdus, est de faire triompher ces valeurs de connaissance et d'humanisme face à la barbarie de nos décideurs. L'histoire de l'infection à VIH a, dans ce sens, été une école qui prouve qu'un certain degré d'activisme doit toujours être maintenu. Il sera notre seul salut face aux maladies émergentes auxquelles nos sociétés seront demain confrontées...
Je vous souhaite un bon séjour à Toulon et un congrès fructueux !

SUMMARY / *SOMMAIRE*

Scientific Program / *Programme scientifique*
Thursday June 3, 2004 / *Jeudi 3 Juin 2004* 6
Friday June 4, 2004 / *Vendredi 4 Juin 2004* 9
Saturday June 5, 2004 / *Samedi 5 Juin 2004* 12

Posters Presentations / *Présentations Posters* 16

Practical Information / *Informations pratiques* 34

Oral Presentation Abstracts
Résumés des communications orales 35

Poster Abstracts / *Résumés des posters* 105

Special Lecture & Workshop Abstracts
Résumés : conférence spéciale & workshop 330

Acknowledgements / *Remerciements* 333

Sponsors / *Partenaires* 335

Thursday June 3, 2004 / *Jeudi 3 Juin 2004*

08.00 am Opening welcome desk / *Ouverture de l'accueil*

Vauban Amphitheater

09.30 am **Session: HIV, Virology** / ***VIH, session virologique***
Chairs : Christine ROUZIOUX, Paris - FRA & Catherine TAMALET, Marseille - FRA

- **OP 1.1.** Recent Data on HIV Resistance to Antiretroviral Drugs
Données récentes sur la résistance aux antirétroviraux
Charles BOUCHER, Utrecht - NED

How to Manage Cross-resistance ? / *Gestion des résistances croisées*

- **OP 1.2.** Resistance to RT Inhibitors / *Résistance aux inhibiteurs de la RT*
Anne-Geneviève MARCELIN, Paris - FRA
- **OP 1.3.** Resistance to PI / *Résistance aux IP*
Luc PERRIN, Geneva - SUI & Denis LACOSTE, Bordeaux - FRA
- **OP 1.4.** Resistance & Reservoirs / *Résistance & réservoirs*
Marie-Laure CHAIX, Paris - FRA
- **OP 1.5.** Rational Prescribing in the Era of HIV Phenotypic Drug Resistance Testing
Hess G, Nelson C, Lipskiy N. Surveillance Data, Plymouth Meeting PA, USA
- **OP 1.6.** Analysis of HIV-2 Resistance to Protease Inhibitors
Nogueira R., Coelho S., Freitas-Vieira A., Mammano F., Goncalves J.
URIA - Unidade de Retrovirologia e Doenças Infecciosas Associadas, University of Lisbon, Faculty of Pharmacy, Lisbon - POR;
Laboratoire de Recherche Antivirale, INSERM U82, Paris - FRA
- **OP 1.7.** Polymorphism and Drug-selected Mutations in the Protease Gene of HIV-1 in Naive and Multi-treated Patient Isolates from the Seine-Saint-Denis District in France: differences between B and non-B subtypes
Hawajri AL., Gault E., Aloui C., Drugan T., Le Gal F., Dziri-Mendil S., Déry P.
Laboratoire de bactériologie, virologie - hygiène, Hôpital Avicenne, AP-HP, EA3406 ATHSCO, UFR SMBH, Université Paris 13, Bobigny - FRA;
University of Medicine and Farmacy, Cluj - ROM

11.00 am Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

11.30 am Workshop / *Atelier*
Future Tendencies in Antiretroviral Therapy
Tendances future du traitement antirétroviral
President: Hervé GALLAIS, Marseille - FRA
Chairmen: François RAFFI, Nantes - FRA & Vincent CALVEZ, Paris - FRA

- **WS 1.1.** PI Cross-resistance / *Gestion des résistances croisées*
- The virologist's point of view / *le point de vue du virologue*
Bernard MASQUELIER, Bordeaux - FRA
- The clinician's point of view / *le point de vue du clinicien*
François RAFFI, Nantes - FRA
- **WS 1.2.** Tipranavir 2004 Update / *Tipranavir : Actualités en 2004*
Laurence WEISS, Paris - FRA
- **WS 1.3.** Tipranavir Compassionate Use and Expanded Access Program
Essai Compassionnel et Accès étendu du programe du tipranavir
Marie-Cécile CAMUS, Reims - FRA

Session in French only

Room Colbert

11.30 am **Meet the Experts Session** / ***Session rencontre des experts***
Genotypic Tests and Drugs Pharmacokinetics in Patients with Treatment Failure: from theory to practice
Intérêt du génotypage et des dosages pharmacologiques dans la prise en charge des patients en échec de traitement : de la théorie à la pratique
Chairman: Gilles PIALOUX, Paris - FRA

- **WS 2.1.** Contribution of Genotypic Tests / *Apport du Génotypage*
Anne-Geneviève MARCELIN, Paris - FRA
- **WS 2.2.** Contribution of Pharmacokinetics / *Apport des dosages pharmacologiques*
Gilles PEYTAVIN, Paris - FRA
- **WS 2.3.** Clinical Cases / *Cas cliniques*
Patient with First Failure of Treatment / *Patient en premier échec de traitement*
Patient with Failure of 3rd or 4th Line of Treatment / *Patient en échec de 3e ou 4e ligne de traitement*
Gilles PIALOUX, Anne-Geneviève MARCELIN, Gilles PEYTAVIN, Paris - FRA

01.00 pm Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

02.00 pm **Session: HIV, Antiretroviral Strategies** / ***VIH, stratégies antirétrovirales***
Chairmen: Stefano VELLA, Roma - ITA & José GATELL, Barcelona - ESP

- **OP 2.1.** Initial Treatment Strategies / *Traitement de première ligne*
Marianne HARRIS, Vancouver - CAN
- **OP 2.2.** New Antiretroviral Strategies / *Nouvelles stratégies antirétrovirales*
Bernard HIRSCHEL, Geneva - SUI
- **OP 2.3.** Managing Therapeutic Failure / *Gestion de l'échec thérapeutique*
Bonaventura CLOTET, Barcelona - ESP
- **OP 2.4.** HIV Resistance & Therapeutic Strategies / *Résistance du VIH & stratégies thérapeutiques*
Carlo Federico PERNO, Roma - ITA
- **OP 2.5.** Effects of Baseline Protease Inhibitor (PI) Mutations on the Efficacy of Ritonavir-Boosted Atazanavir (ATV/RTV) and Lopinavir/Ritonavir (LPV/RTV) in Patients Who Have Experienced Virologic Failure on Multiple HAART Regimens
JOHNSON MA, London - UK

Vauban Amphitheater

03.00 pm **Symposium GILEAD Sciences**
Simplifying Antiretroviral Strategies: limits and benefits
Simplicité des stratégies antirétrovirales : limites et bénéfices
Chairman: Alain LAFEUILLADE, Toulon - FRA

- **SS 1.1.** Triple NUC Combinations: real life clinical experience *versus* recently presented data
Trithérapies de NUC : confrontation d'une expérience clinique aux données récentes publiées
Jean-Marie LANG, Strasbourg - FRA
- **SS 1.2.** Is Regimen Simplication Compatible with Effectiveness?
Impact de la simplicité sur la puissance des traitements antirétroviraux
Bonaventura CLOTET, Barcelona - ESP
- **SS 1.3.** Update on Tenofovir Pharmacology
Dernières données de pharmacologie de Ténofovir
Caroline SOLAS, Marseille - FRA

04.30 pm Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

05.00 pm **Session: HIV, Immunology** / ***VIH, immunologie***
Chairmen: Giuseppe PANTALEO, Geneva - SUI & Jean-François DELFRAISSY, Paris - FRA

- **OP 3.1.** HAART-induced Immune Reconstitution: limitations & prospects
Reconstitution immune induite par la trithérapie : limitations & perspectives
Giuseppe PANTALEO, Geneva - SUI
- **OP 3.2.** New Insights into Immune Reconstitution / *Actualités dans la reconstitution immune*
Marie-Lise GOUGEON, Paris - FRA
- **OP 3.3.** State of the Art of anti-HIV Immunotherapy / *Etat des lieux de l'immunothérapie anti-VIH*
Giuseppe TAMBUSSI, Milano - ITA
- **OP 3.4.** The Future of HIV Vaccine Development / *L'avenir de la recherche vaccinale*
Richard KOUP, Bethesda - USA
- **OP 3.5.** Humoral Immune Response Monitoring in HIV-1-infected Patients under anti-Tat Therapeutic Vaccine Trials
Zagury D., Le Buanec H., Badran BM., Willard-Gallo KE., Burny A. and Gallo RC.
Université P. et M. Curie; Néovacs, Paris; ULB, Bruxelles; Institute of Human Virology, Baltimore - USA

06.00 pm Welcome message / *Message de bienvenue*

Vauban Amphitheater

06.05 pm **Special Lecture** / ***Conférence spéciale***
- **SL 1.1.** HIV Reservoirs: implications for therapy
Réservoirs du VIH : implications thérapeutiques
Roger POMERANTZ, Philadelphia - USA

06.30 pm Welcome cocktail in the exhibition / *Cocktail de bienvenue dans l'exposition*

Friday June 4, 2004 / *Vendredi 4 Juin 2004*

Vauban Amphitheater

08.30 am **Session: HIV, Pharmacology & New Drugs**
VIH, session pharmacologique & nouvelles thérapeutiques
Chairmen: Gilles PEYTAVIN, Paris - FRA & Caroline SOLAS, Marseille - FRA

- **OP 4.1.** Optimal Use of Therapeutic Drug Monitoring in ARV Therapy
Utilisation optimale du suivi pharmacologique des antirétroviraux
David BURGER, Amsterdam - NED
- **OP 4.2.** The Search for New Antiretroviral Drugs / *Recherche de nouveaux antirétroviraux*
Erik DE CLERCQ, Leuven - BEL
- **OP 4.3.** New Antiretrovirals in the Gilead Pipeline / *Molécules développées par Gilead*
Jim ROONEY, Foster City - USA
- **OP 4.4.** TMC114: a new PI / *TMC114 : nouvel inhibiteur de protéase*
Eric LEFEBVRE, Yardley - USA
- **OP 4.5.** UK 427, 857: a promising new drug / *UK 427, 857 : nouvelle molécule prometteuse*
Chris HITCHCOCK, Sandwich - GBR
- **OP 4.6.** BMS 488043: a new HIV attachment inhibitor
BMS 488043 : nouvel inhibiteur d'attachement du VIH
Richard COLONNO, Wallingford - USA
- **OP 4.7.** PA 457: a novel anti-HIV drug candidate / *PA 457 : nouveau candidat anti-VIH*
Carl WILD, Gaithersburg - USA
- **OP 4.8.** SPD 754: a new RTI / *SPD 754 : nouveau RTI*
Richard BETHELL, Laval, Québec - CAN

10.30 am Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

11.00 am **Symposium Bristol-Myers Squibb**
A New Protease Inhibitor in Antiretroviral Strategies
Place d'un nouvel inhibiteur de protéase dans la stratégie de prise en charge
Chaimen: Alain LAFEUILLADE, Toulon - FRA & Françoise BRUN-VEZINET, Paris - FRA

- **SS 2.1.** Atazanavir Clinical Data / *Données cliniques d'un nouvel inhibiteur de protéase : Reyataz*
Roland LANDMAN, Paris - FRA
- **SS 2.2.** Atazanavir & Sensitivity Profile / *Reyataz & profil de sensibilité*
Richard COLONNO, Wallingford - USA
- **SS 2.3.** Pharmacokinetics Rationale for once-a-day Treatment
Prise unique quotidienne : pré-requis pharmacocinétiques
Thibaut LAVRUT, Nice - FRA
- **SS 2.4.** Which Factors to Consider for Managing Patients in 2004?
Facteurs déterminants dans la prise en charge thérapeutique des patients
Isabelle POIZOT-MARTIN, Marseille - FRA

12.30 pm Lunch, courtesy of Bristol-Myers Squibb / *Déjeuner offert par Bristol-Myers Squibb*

Vauban Amphitheater

02.00 pm **Session: HIV, HAART Adverse Effects / *VIH, effets secondaires de la trithérapie***
Chairmen:
Pascale LECLERCQ, Grenoble - FRA & Alain LAFEUILLADE, Toulon - FRA

- **OP 5.1.** Management of Metabolic Complications of Antiretroviral Therapy
  Gestion des complications métaboliques du traitement antirétroviral
  Morrie SCHAMBELAN, San Francisco - USA
- **OP 5.2.** Update on HAART-induced Lipodystrophy
  Actualités sur la lipodystrophie induite par les antirétroviraux
  Jacqueline CAPEAU, Paris - FRA
- **OP 5.3.** In vitro Suppression of the Lipogenic Pathway by the non-nucleoside Reverse Transcriptase Inhibitor Efavirenz in 3T3 and Human Preadipocytes or Adipocytes
  El Hadri K., Glorian M., Monsempes C., Dieudonné MN., Pecquery R., Giudicelli Y., Andreani M., Dugail I., Fève B. UMR CNRS 7079, Paris - FRA

■ Panel Discussion / *Discussion avec les experts*
Pascale LECLERCQ, Grenoble - FRA, Alain LAFEUILLADE, Toulon - FRA,
Morrie SCHAMBELAN, San Francisco - USA, Jacqueline CAPEAU, Paris - FRA

Vauban Amphitheater

03.00 pm **Symposium Roche**
Place of Fusion Inhibitors in Therapeutic Strategies
Place des inhibiteurs de fusion dans les stratégies thérapeutiques
Chairman: Hervé GALLAIS, Marseille - FRA

- **SS 3.1.** Virological Data / *Données virologiques*
  Jean-Claude TARDY, Lyon - FRA
- **SS 3.2.** 1st Clinical Case / *1er Cas Clinique*
  Alain LAFEUILLADE, Toulon - FRA

• Discussion
Alain LAFEUILLADE, Toulon - FRA
Jean-Claude TARDY, Lyon - FRA
Rodolphe GARRAFFO, Nice - FRA

- **SS 3.3.** 2nd Clinical Case / *2e Cas Clinique*
  Laurent COTTE, Lyon - FRA

• Discussion
Laurent COTTE, Lyon - FRA
Jean-Claude TARDY, Lyon - FRA
Rodolphe GARRAFFO, Nice - FRA

- **SS 3.4.** Guidelines / *Directives*
  François RAFFI, Nantes - FRA

■ Questions-Answers / *Questions-Réponses*

Best Poster Award by Roche Laboratory / *Remise du prix poster par le Laboratoire Roche*

04.30 pm Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

05.00 pm **Special Lecture / *Conférence spéciale***
- **SL 1.2.** New Concepts in anti-HIV Therapy / *Nouveaux concepts du traitement anti-VIH*
  Robert GALLO, Baltimore - USA

Room Colbert

05.30 pm **Investigators Kaleobs Meeting / *Réunion Investigateurs Kaleobs***
On invitation only / *Sur invitation uniquement*

ABBOTT.VIH

Vauban Amphitheater

05.30 pm **Session: HIV in a Widened Europe / *VIH dans une Europe élargie***
Chairmen: Yves MOUTON, Tourcoing - FRA & Emmanuel DELBEKE, Toulon - FRA

- **OP 6.1.** HIV in Central & Eastern Europe
  VIH en Europe Centrale et Europe de l'Est
  Caroline SEMAILLE, Paris - FRA
- **OP 6.2.** Family Systems for Substance Abuse & HIV Care in Ukraine
  Systèmes de prise en charge en Ukraine
  Natalia VLASOVA, Vinnitsa - UKR
- **OP 6.3.** HIV Infection in Estonia
  Infection VIH en Estonie
  Anneli UUSKULA, Tartu - EST
- **OP 6.4.** STDs in Slovakia
  ISTs en Slovaquie
  Emil TOMASIK, Bratislava - SLO
- **OP 6.5.** The Incidence of Viral Hepatitis Markers among Romanian Teenagers with Long-lasting Horizontally Acquired HIV Infection
  Ruta S. Institute of Virology, Bucharest - ROM

Saturday June 5, 2004 / *Samedi 5 Juin 2004*

Vauban Amphitheater

08.15 am **Session: Viral Hepatitis / *Hépatites virales***
Chairmen: Jean-Marie LANG, Strasbourg - FRA & Vicente SORIANO, Madrid - ESP

- **OP 7.1.** Treatment of HIV-HBV Coinfection
Traitement de la coinfection VIH-VHB
Yves BENHAMOU, Paris - FRA

- **OP 7.2.** Treatment of HIV-HCV Coinfection
Traitement de la coinfection VIH-VHC
Vicente SORIANO, Madrid - ESP

- **OP 7.3.** Tolerance of Viral Hepatitis Therapy in HIV-infected Patients
Tolérance du traitement des hépatites virales chez les patients infectés par VIH
Gilles PIALOUX, Paris - FRA

- **OP 7.4.** Role of the Hepatitis C virus-coinfection on Humoral Immune Alterations in HIV-infected Patients on HAART
Soriano-Sarabia N., Molina-Pinelo S., Delgado-Pecellin C., de Felipe B., Sanchez-Quijano A., Lissen, Leal EM., Vallejo A.
Group for the Study of Viral Hepatitis and AIDS,
Hospital Universitario Virgen del Rocio, Seville - SPA

- **OP 7.5.** Liver Transplantation in Five HIV-infected Patients With Virus Hepatitis Induced Cirrhosis
Radecke K., Frühauf NR., Miller M., Ross B., Köditz R., Malago M., Treichel U., Broelsch CE., Gerken G.
Department of Gastroenterology and Hepatology, Department of General Surgery and Transplantation, University Hospital Essen, Essen - GER

09.45 am Break, Posters, Exhibition / *Pause, posters, exposition*

Room Colbert

10.15 am **Session: Free oral Presentations, Basic Science / *Communications libres***
Chairmen:
Jean-Pierre de JAUREGUIBERRY, Toulon - FRA & Catherine TAMALET, Marseille - FRA

- **OP 8.1.** NF90ctv, a cellular dsRNA binding Protein Inhibits the Rev-dependent Export of HIV-1 RNA
Castaño ME; Kumar A and Urcuqui-Inchima S. Immunovirology Laboratory, Faculty of Medicine, University of Antioquia, Medellin - COL

- **OP 8.2.** Expression of HIV-1 gp160 in Transgenic Animals.
Berrada F., Al Akhawayn University in Ifrane. School of Science & Engineering, Ifrane - MAR

- **OP 8.3.** Polymorphisms in CCR5 promoter are associated with rare HIV-1 infection of the D32/D32 homozygous individuals
Xihau Lu, Ghalib Alkhatib, R. Tubiana and L. Meyer.
Indiana University School of Medicine, Indianapolis, Indiana - USA

- **OP 8.4.** Evaluation of Porcine Thymic Xenografts to Restore Human Thymopoiesis that is Resistant to HIV Infection
Hadidi S., Damrauer S., Lan P., Yang YG., Sykes M.
Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

- **OP 8.5.** Pol mutations and polymorphisms associated with NRTI and NNRTI-based regimens in Botswana patients infected with HIV-1 C.
Doualla-Bell F., Gaseitsiwe S., Ndung'u T., Modukanele M., Peter T., Novitsky V., Ndwapi N., Gaolathe T., Avalos A., Wester W., Bussmann H., Cardiello P., Marlink R., Moffat H., Thior I., Essex M., Wainberg MA.
McGill AIDS Centre- McGill University, Montreal, Canada; Botswana Harvard Partnership for HIV Research and EducationGaborone, Botswana, Harvard School of Public Health, Boston - USA

- **OP 8.6.** Aminoglycoside-arginine Conjugates: chemical barriers of HIV-1 entry
Lapidot A and Borkow G. Department of Organic Chemistry, Weizmann Institute of Science, Rehovot - ISR

- **OP 8.7.** Pharmacological Blockade of Receptors Connecting To Inhibitory Pathways Of Immune Cells May Be An Efficient Immunopotentiating Treatment Of HIV/AIDS
Peuschel KE. Independent Researcher, Lugano - SUI

- **OP 8.8.** Structure of Viral Antitermination Complexes
Schwarz S., Scheckenhofer U., Prasch S., Eisenmann A., Schweimer K., Wöhrl B., & Rösch P. Lehrstuhl für Biopolymere, University, Bayreuth - GER

- **OP 8.9.** The VirtualPhenotypeTM Analysis of an HIV-1 Genotype Provides a More Accurate Prediction of Drug Susceptibility Than a Single Phenotype Measurement
Van Houtte M., Vermeiren H., Lecocq P., Winters B., Pattery T., Mc Kenna P., Bacheler L.
Virco BVBA, Mechelen, Belgium; VircoLab Inc, Durham, NC - USA

Vauban Amphitheater

10.15 am **Session: Free Oral Presentations Clinical Sciences / *Communications libres***
Chairmen: Jean-Albert Gastaut, Marseille - FRA & Alain Lafeuillade, Toulon - FRA

- **OP 9.1.** Chinese SARS and AIDS Control at Frontier Ports
Mingchang S., Yonggui L., Yuping H. Madiandonglu Haidian District Beijing. P.R. - CHN

- **OP 9.2.** HIV-1 subtypes in the Northern Border Region of Kenya
Lihana RW,Lwembe RM, Kiptoo MK, Ochieng W, Oishi I, Ichimura H, Songok EM.
Kenya Medical Research Institute, Jomo Kenyatta University of Technology, KEMRI/JICA Project, Nairobi - KEN

- **OP 9.3.** Method of Treatment of Acquired Immune Deficiency Syndrome with Embryonic Hempatopoietic Stem Cells
Smikodub OI. Cell Therapy Clinic of National Medical University and Embryonic Tissues Center EmCell - UKR

- **OP 9.4.** Andrieu Unjustly Disregarded. Better CD4-counts with Prednisolone
Ulmer, Albrecht; Mueller, Markus; Frietsch, Bernhard. HIV-Practice, Stuttgart - GER

- **OP 9.5.** Enhanced Immunogenicity of HIV-1 Whole Killed Vaccine in Association with Amplivax™
  Trabattoni D, Clivio A, Gori A, Bartholomew R, Fernandez-Cruz E, Lowry P, Kandimalla ER, Sullivan T, Bhagat L, Agrawal S, Clerici M, TheofanG, Bray DH. Dept Immunol, Dept Biol, Milano University, Dept Infect Dis, Milano, Italy; MRC Clinical Trials Unit, London, UK; Gregorio Maraon Univ Hospital, Madrid, Spain; Hybridon, Inc, Cambridge, Immune Response Co, Carlsbad - USA

- **OP 9.6.** ESAT-6 and CFP-10 derived peptides for diagnosis of TB infection in severely immuno compromized HIV-infected individuals
  Fortis C, Tasca S, Mantegani P, Lazzarin A, Scarpellini P. IRCCS San Raffaele, Milano - ITA

- **OP 9.7.** Why the Patient's Perspective is Critical in the Management of Lipodystrophy?
  Duracinsky M, Cervoni J, Bourgarit A, Sereni D, Molina JM, Wu A, Chassany O. Hopital de Bicêtre; Hopital Lariboisiere, Hopital Saint-Louis, Paris, France; Johns Hopkins University, Baltimore - USA

- **OP 9.8.** A Technological Monitoring and Management-Support System for Anti-Retroviral Therapy in South Africa: Introducing Cell-Life
  S. Anand, U. Rivett, Cell-Life, University of Cape Town - South Africa

Vauban Amphitheater

12.00 pm **Session: Update on SARS /** ***Mise au point sur le SRAS***
Chairmen: Alain LAFEUILLADE, Toulon - FRA & Gilles HITTINGER, Toulon - FRA

- **OP 10.1.** SARS: past, present, future / *SRAS : passé, présent, avenir*
  Tao HUNG, Beijing - CHN

- **OP 10.2.** Clinical Management of Patients with SARS / *Prise en charge des cas de SRAS*
  Joe SUNG, Hong Kong - CHN

- **OP 10.3.** The SARS-CoV S Glycoprotein, Mediator of Entry, Vaccine Immunogen and Target for Drugs / *La glycoprotéine CoV S du virus du SRAS, médiateur d'entrée, cible vaccinale et médicamenteuse*
  Dimiter DIMITROV, Frederick - USA

- **OP 10.4.** Detection & Quantification of the SARS-associated Coronavirus
  Détection & quantification du coronavirus responsable du SRAS
  Leondios KOSTRIKIS, Nicosia - CYP

- **OP 10.5.** Concentration and Detection of SARS Coronavirus in Sewage from Xiao Tang Shan Hospital and the 309th Hospital of the Chinese PLA
  Li J, Wang XW, Chao FH, Li J, Zhen B, Kong Q, Son N, Jin M, Xiao W, Gu C, Yin J, Wei W. Institute of Hygiene and Environmental Medicine, Academy of Military Medical Sciences, P.R. China; Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, P.R - CHI

- **OP 10.6.** Purification, Characterization, and Immunogenicity of a Truncated Form of the SARS Spike Protein: Toward a recombinant glycoprotein subunit vaccine
  Kan E, Coates S, Stadler K, Matsuoka K, Calderon E, Song H, Seo MY, Wininger M, Barnett S, Ulmer J, Rappuoli R, Abrignani S, Houghto, M, Han J, Srivasta I. Chiron Corporation, Emeryville, USA; IRIS, Chiron S.r.l., Siena - ITA

01.00 pm Break, Posters, Exhibition / *Pause, posters, exposition*

Vauban Amphitheater

02.15 pm **Session: Concerns in HIV Care /** ***Inquiétudes dans la prise en charge du VIH***
Chairmen: Alain LAFEUILLADE, Toulon - FRA & Alain RIEU, Toulon - FRA

- **OP 11.1.** AIDS in Africa: a terrible injustice
  Le SIDA en Afrique : une terrible injustice
  Marie-José MBUZENAKAMWE, Bujumbura - BDI

- **OP 11.2.** Has HIV Prevention some Efficacy in the Developed World?
  La prévention du VIH est-elle efficace dans les pays développés ?
  Didier LESTRADE, Paris - FRA

- **OP 11.3.** HIV no longer a Disease Apart?
  Le VIH perd-il le statut de maladie particulière ?
  Gilles PIALOUX, Paris - FRA

- **OP 11.4.** Economic Threats on Fundamental Research
  Menaces économiques sur la recherche fondamentale
  Jean-Louis VIRELIZIER, Paris - FRA

  - Panel & Participants Discussion / *Discussion entre les orateurs & les participants*

03.30 pm **Session: Poster Discussion /** ***Discussion de Posters***
Several posters in each track will be selected by the Scientific Committee and discussed with the participants & authors / *Plusieurs posters dans chaque thème seront sélectionnés par le Comité Scientifique et discutés avec les participants et leurs auteurs*

04.30 pm Closing / *Clôture*

HIV, Epidemiology

- **PP 1.1** Trends in the HIV/Aids Epidemic in Women in the City of São Paulo, 1985 - 2000
  Tancredi MV, Waldman EA. Referral and Trainning Centers for STD/Aids - São Paulo, Sao Paulo - Brazil

- **PP 1.2** Les Jeunes Parlent aux Jeunes.
  Diatta A, Ndiaye MA, FALL MF. Groupe Communication Internationale en Technologie Cultures et Services en Afrique (G.CITCS Afrique), Dakar - Senegal

- **PP 1.3** Serological Profiles in Hemodialysed Patients of Constantine
  Semra Z, Ait Kaki B, Boulkhdra A.
  Laboratoire de Microbiologie CHU Constantine - Algeria

- **PP 1.4** Sero-epidemiological aspects of the HIV infection in Algeria
  Ait Kaki B, Belabbes E, Bouguremouh A. Laboratoire de Microbiologie CHU Benbadis, Constantine & Institut Pasteur Virologie, Alger - Algeria

- **PP 1.5** Surveillance of HIV/AIDS. Epidemiological Trends. Cuba: 1986-2003
  Torres Peña R, Joanes Fiol JJ, Lantero Abreu MI, Estévez G.
  Ministry of Public Health, National Aids Program, Havana City - Cuba

- **PP 1.6** The Vertical Transmission of the Pediatric AIDS in Cuba
  González I, Díaz M, Pérez J. Instituto Pedro Kouri Ciudad Habana - Cuba

- **PP 1.7** Correlation of HIV Prevalence Rates Between Sexually Transmitted Diseases Patients And Pregnant Women Attending Antenatal Clinic In India
  Kant S, Shaukat M. All India Institute of Medical Science, National AIDS Control Organisation, New Delhi - India

- **PP 1.8** The Rate of HIV/AIDS from 1987 to 2003 in Belarus and Influence of Injecting Drug Users on the Expansion of HIV Infection
  Kaskevich IA. Vitebsk State Medical University - Belarus

- **PP 1.9** HIV Infection: present persisting problems for pregnant women and their babies and families
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 1.10** Temporal Trend of Fatality Events in a Cohort of 1,214 Heroin Drug Addicts Followed Since 1977 in Bologna, Italy. Role and evolution of HIV-associated deaths
  Manfredi R, Sabbatani S, AgostiniD, Chiodo F. Infectious Diseases, University of Bologna, and Department of Public Health, Bologna - Italy

- **PP 1.11** Introduction to Risk Mapping and Behavioural Analysis as Tools to Fight against STI/HIV/AIDS: the case of Douala Cameroon
  Jeanne d'Arc KENGNE. Association Culturelle Mission de Recréation (ACMR), Douala - Akwa Douala - Cameroon

- **PP 1.12** Pluses of HIV/AIDS Peer education Training For Adolescents In Uganda.; A Case of the AIDS Challenge Youth Club
  Sentamu SPS, Lukwago BL.The AIDS Support Organisation, Kampala - Uganda

- **PP 1.13** Health Seeking Behaviour-Means of Stimulating Youth Into Seeking It?
  Sentamu SPS.The AIDS Support Organisation, Kampala - Uganda

- **PP 1.14** The Professional Insertion of AIDS-infected Young Girls
  Muyuku EM, Munyana MM.Swaa-Burundi, Bujumbura - Burundi

- **PP 1.15** The Role of Religious Doctrines in Prevention of AIDS
  Esmaeelzadeh M, Ghanbari M. Mashhad University of Medical Sciences, Mashhad - Iran

- **PP 1.16** The Role of IV Drug Users´s Control in Prevention of AIDS
  Ghanbari M, Esmaeelzadeh M. Mashhad University of Medical Sciences, Mashhad - Iran

- **PP 1.17** Screening of Iranian Blood Donors for Transfusion Transmitted Infections
  Moniri R., Mossavi G.A. Kashan University of Medical Sciences - Iran

- **PP 1.18** Prostituées de Rue et VIH : interactions sexuelles et logiques de gestion du risque.
  Trottier G, Damant D, Paré G, Doitteau N, Noël L, et Michel Dorais
  Laval University, School of Social Work, Québec - Canada

- **PP 1.19** Sexual Behaviour of Female Undergraduates in the Freshman Year at the University of Ibadan, Nigeria
  Faseru B, Sangowawa AO, Okoro CA, Lawoyin TO.
  University College Hospital, Ibadan - Nigeria

- **PP 1.20** Epidemiological Features of Tuberculosis in Northern Italy, and Public Health Care Correlates
  Manfredi R, Sabbatani S, Legnani G, Chiodo F
  Infectious Diseases, University of Bologna - Italy

- **PP 1.21** International Charity Organization "Rehabilitation Center "STEPS", Vinnitsa branch, Ukraine, Activities.
  Vlasova N.
  Vinnitsa Branch of International Charity Organization "Steps", Vinnitsa - Ukraine

- **PP 1.22** Evolving Assistance Features at an Infectious Disease Day-Hospital Service, in Relation with the Natural History of HIV Infection in the Highly Active Antiretroviral Therapy (HAART) Era
  Manfredi R, Calza L, Chiodo F
  Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 1.23** To Foster Awarness Against AIDS
  Sarker AH. Physiotherapy Center, Dhaka, Bangladesh

- **PP 1.24** Immigration and HIV Infection in Northern Italy. Inpatient Admissions, 2000-2003
  Manfredi R, Calza L, Chiodo F
  Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 1.25** Disasters on Medications and Technical Behaviour Condition
  RoseJoshi. Kathmandu - Nepal

- **PP 1.26** Stigma Attached to HIV / AIDS : Implications for Health Care and Social Adjustment in Mumbai
  Chauhan SL. National Institute for Research in Reproductive Health, Mumbai - India

- **PP 1.27** The Problems and Effects of Mother to Child (MTC) HIV Transmission in an Extended Family System in Ghana. Duodu MO, Osei-Ntim O, Agyekum D, Afriyie KO, Amponsah G.
  Beware of AIDS (BAWA), Manchester - UK

- **PP 1.28** The Economic and Educational Problems of HIV/AIDS' Infection in Rural Ghana
  Duodu MO, Mohammed MY, Osei-Ntim O, Adusei K, Amponsah G. Beware of AIDS (BAWA), Manchester - UK

- **PP 1.29** Premarital Sex Towards Infertility and STD'S Infection
  Smith C. Kwadaso-Kumasi - Ghana

- **PP 1.30** A Bridge of HIV Transmission Between Injection Drug Users and General Population in Ukraine
  Kyrychenko PD, Vlasova N. Vinnitsa Pirogov National Medical University, International Charity Organization "STEPS", Vinnitsa branch, Vinnitsa - Ukraine

- **PP 1.31** Trends in HIV Risk Behaviors in Castellon, Spain
  Roca B, Ventura JM, Tornador N, Bahamonde D. Hospital General of Castellon - Spain

- **PP 1.32** Multi Drug Resistant Tuberculosis (MDR-TB) And Public Health Policy
  Atre SR. The Foundation for Research in Community Health, Pune - India

- **PP 1.33** Reducing and preventing HIV/AIDS and other STIs incidence and prevalence among cross-cultural groups in South Florida, Haiti and Jamaica: A Tri National Project.
  Delva F, Fanfan MF. Florida International University, Florida Memorial College, Miami, University of South Florida, Tampa, Florida - USA

- **PP 1.34** Factors Associated with Continuation of High-risk Behaviour by HIV-positive Injection Drug Users
  Kyrychenko P. Vinnitsa Pirogov National Medical University, Vinnitsa - Ukraine

- **PP 1.35** Lost Opportunities of Detection of HIV Infection during Pregnancy in Brazil
  Szwarcwald CL. Fundação Oswaldo Cruz, Rio de Janeiro - Brazil

- **PP 1.36** Prise en Charge des Enfants Orphelins du SIDA
  Jacquie Militoni. Santé et Développement Communautaire, RDC

- **PP 1.37** Infant Feeding in the Context Of HIV/AIDS: a Call to Action
  Liles C, Tompson M. AnotherLook, Evanston, Illinois - USA

- **PP 1.38** Surveillance study of selected sexually and blood transmitted infections in HIV-negative vs. HIV-positive pregnant women and their newborns in SR.
  Stanekova D, Adamcakova J, Kopilcova T, Kotuliak J, Vaculikova E, Habekova M, Mokras M. Slovak Health University, Bratislava - Slovakia

- **PP 1.39** Mobilisation des Femmes Infectées et Affectées par le VIH/SIDA pour une Large Réponse à l'Epidémie
  Outiama P. Dpt Santé, PVVS, Bangui, RCA

- **PP 1.40** Public health surveillance of sexual exposure to HIV in the French Armed Forces in 2002
  Michel R, Ollivier L, Aiesi F, Meynard JB, Boutin JP. IMTSSA, Marseille - France

- **PP 1.41** Guaranteed Education on Safe Sex and HIV Related Infections for Cameroonians in Relation to Blood Donation: Itoe F, Natural Initiative for Voluntary Blood Donors - Cameroon

- **PP 1.42** Prevalence of HCV Specific antibody, RNA and genotypes among HIV infected Iraqi haemophiliacs : Al-Kubaisy WA, Al-Nahrain University/Medical College, Baghdad - Iraq

- **PP 1.43** HIV/AIDS, STI Prevention And Sex Education In Nepalese Schools/Colleges Youths : Gautam R, Koirala M. BP Memorial Health Foundation, New Baneshwor - Kathmandu, Nepal

- **PP 1.44** The women's antenatal care initiative for reduction of HIV mother-to-child transmission in Colombia - The Mother & Child Project - (project funded by the European Commission) :
  García Bernal R, Arenas Granada CD, Prieto Alvarado FP, Rincón Ramirez JA, Vargas LE, Ramirez Ramirez CM. UNAIDS, Bogotá - Colombia

- **PP 1.45** Prevalence of Drug-Resistant HIV Mutants In Recently Infected And Naïve Patients In Liguria, A North-Western Region of Italy: Setti M, Bruzzone B, Ventura A, Murdaca G, Frabetti M, Icardi G, Indiveri F. Department of Internal Medicine, Department of Health Sciences, University of Genoa, Genoa - Italy

- **PP 1.46** Occupational Exposure to HIV, HBV and HCV Among S. Martino Hospital Health Care Workers (Genoa) in the Years 1989 To 2003: Setti M, Cardinale F, Riccio C, Sticchi C, Talassio G, Frabetti M, Icardi G, Bruzzone B. Department of Internal Medicine, Department of Health Sciences, University of Genoa, Genoa - Italy

- **PP 1.47** Ethics in the Information: Silva HMS. University of Itaúna, Itaúna, Faculty of Formiga, Formiga , Faculty of Pará de Minas, Pará de Minas - Brazil

- **PP 1.48** Knowledge, Perception And Acceptability Of Microbicides (KPA) Among Non-health Care Givers In Lagos, Nigeria: Smith SI, Agomo C, Idigbe EO
  Nigerian Institute of Medical Research, Lagos - Nigeria

- **PP 1.49** Lubricants Containing N-9 May Enhance Rectal Transmission of HIV and Other STIs:
  Phillips D, Sudol K, Taylor C, Guichard L, Elsen R, Maguire R
  Population Council, New York & Sexual Health project, San Francisco - USA

- **PP 1.50** HIV/AIDS As a Part of Health Policy - Acceptance
  Lakhani A, Saiyyad YA. Deepak Charitable Trust, Vadodara - India

- **PP 1.51** HIV/AIDS & Women's Economic Empowerment
  Lakhani A. Deepak Charitable Trust, Vadodara - India

- **PP 1.52** HIV/AIDS Care And Support Program
  Annapoorni TM, Roberts VA, MacDonald LC. BLOSSOM, Virudhunagar - India

- **PP 1.53** Coinfection of Hepatitis B and Hepatitis C Virus among HIV Patients in Ho Chi Minh City Vietnam
  Vo TTN, Nguyen HC, Maynart M, Nguyen VN, Ngo TKC, Pham VH, Truong XL, Follezou JY. Tropical Medicine Hospital, Pasteur Institute in Ho Chi Minh city, Binh Trieu Hospital, Preventive Medicine Center, Ho Chi Minh, Vietnam; University of Paris VI, Paris - France

- **PP 1.54** Mentality of PLWH/A and Affected Families in the Slum-based Poorest of Poor Community
  Swamy G, Bansode S. John Paul Slum Development Project, Pune - Indonesia

- **PP 1.55** Demographics of HIV Patients Referred for Initial Visits to a NYC Clinic
  Jin S. Suh, Kinga Chieloszyk, Robert Warford, Phyllis Ristau, Victoria Sharp, New York - USA

- **PP 1.56** Homosexuality and HIV/AIDS in Kathmandu, Nepal:
  Pkhakadze G. University of Madras, Department of Anthropology, Chennai - Nepal

HIV, HCV, Basic Science

- **PP 2.1** The Core Protein of Hepatitis C Virus is a Potent RNA Chaperone Promoting Dimerization of the Viral Positive-Strand RNA
  Ivanyi-Nagy R, Cristofari G, Gabus C, Boulant S, Lavergne JP, Penin F, Darlix JL
  LaboRetro, INSERM U412, ENS de Lyon, IBCP CNRS, Lyon - France

- **PP 2.2** The Design of HIV-1 Infection Laboratory Model in Cotton Rats
  Rytik PG, Kutcherov II, Muller WEG, Poleshchuk NN
  Research Institute, Minsk - Bielarus

- **PP 2.3** A Newly Developed Provirus Quantification Assay using Real-time SYBR Green I PCR and its Validation in a Murine AIDS Model
  Casabianca A, Orlandi C, Fraternale A and Magnani M. Institute of Biological Chemistry "Giorgio Fornaini", University of Urbino, Urbino (PU) - Italy

- **PP 2.4** Different Mechanisms of HIV-1 RT-mediated Homologous and Non-homologous Recombination
  Kurzynska-Kokorniak A, Jankowska A, Jackowiak P, Alejska M, Figlerowicz M
  Institute of Bioorganic Chemistry Polish Academy of Sciences, Noskowskiego, Poznan - Poland

- **PP 2.5** Influence of Antigenic Peptide Structure and Delivery System on the Level and Polarization of Immune Response
  Maksyutova AV, Bulychev LE, Maksyutov AZ, Poryvaev VD, Lebedev LR, Ryzhikov AB.
  SRC VB "Vector", Koltsovo, Novosibirsk - Russia

- **PP 2.6** Identify the Cellular Factors that Interact with Retrovirus Receptors using Yeast-Two Hybrid System
  Rezvan M, Tailor CS, Kashan University of Medical Sciences - Iran

- **PP 2.7** HIV-1 5'UTR Functions as a Ryboswitch Regulating Genomic RNA Replication and Recombination
  Urbanowicz A, Jankowska A, Berkhout B, Figlerowicz M. Institute of Bioorganic Chemistry Polish Academy of Sciences, Noskowskiego, Poznan - Poland

- **PP 2.8** A Novel CCR5 Mutation Selectively Affects Immunoreactivity and Fusogenic Property of the HIV Co-receptor in a Slow Progressing HIV Patient
  Zhao XY, Lee SS, Wong KH, Chi-Wai Chan K, He ZM, Ma S, Chung-Sing Chan C, Mun-Hon Ng, Zheng BJ
  HIV Research Laboratories, Department of Microbiology, the University of Hong Kong; Integrated Treatment Centre, Department of Health; Hong-Kong - China

- **PP 2.9** The P40 ORF1 Product of The Human LINE-1 Retrotransposon Possesses Sequence Similarities To HIV-1 Gag
  Zhou JL, Kim SJ, Kirou KA, Crow MK. Hospital for Special Surgery, New York - USA

- **PP 2.10** Automation of Sample Preparation for Quantitative HIV RNA PCR LCx assay
  Muller Z, Stelzl E, Kessler HH.
  Department of Clinical Microbiology, Szekesfehervar, Hungary, Molecular Diagnostic Laboratory, Institute of Hygiene, KF-University, Graz - Austria

- **PP 2.11** Intracellular Concentration of Indinavir (IDV) in Patients with AIDS Receiving Two Different Dosages of Indinavir/ritonavir (IDV/rtv)
  Garraffo R, Lavrut T, Simonet P and Pugliese P
  Nice University Hospital and Cannes General Hospital - France

- **PP 2.12** Effect of HIV Protease Inhibitors on P-glycoprotein Expression in Peripheral Blood Mononuclear Cells: an in vivo and in vitro study.
  Le Saint C, Charnay Y, Lafeuillade A, Vincent JP and Cupo A
  Institut de Pharmacologie Cellulaire et Moléculaire UMR-CNRS 6097, Valbonne, france; Hôpitaux Universitaires de Genève, Division de Neuropsychiatrie, Genève, Suisse; Unité Infectiologie, Hôpital Chalucet, rue Chalucet, Toulon - France

- **PP 2.13** The intracellular content of phosphorylated metabolites of AZT and d4T may be quantified in HIV infected patients by two independant specific immunoassays .
  Le Saint C, Menguy V, Lafeuillade A, Vincent JP and Cupo A. Institut de Pharmacologie Cellulaire et Moléculaire UMR-CNRS 6097, Valbonne; Unité Infectiologie, Hôpital Chalucet, rue Chalucet, Toulon - France

- **PP 2.14** Low Impact of MDR1 Genotype on the Pharmacokinetic (PK) Parameters of Indinavir (IDV) in HIV-Infected Patients Treated or Not with Low-dose Ritonavir (RTV)
  Solas C, Poizot-Martin I, Simon N, Bourgarel-Rey V,Dinh T, Sampol-Manos E, Villard PH, Gastaut JA, Lacarelle B.Timone Hospital, Sainte-Marguerite Hospital, UMR-CNRS 6032, University of Mediterannee, Marseille - France

- **PP 2.15** CD4 and CD14 Receptors Down-modulation by Potent Microbicide Lithium-Iodophore
  Davtyan TK, Hakobyan IS, Gabrielyan ES
  CJSC "Armenicum" Clinical Centre, Yerevan - Armenia

- **PP 2.16** HIV-1 decoy TAR and vif siRNA Expressed as a Single RNA Molecule under the Human U6 Promoter Enhanced the Inhibition Efficacy of HIV-1 Replication in Transduced Cells.
  Barnor JS, Miyano-Kurosaki N, Abumi Y, Shiina H, Ishikawa K, Yamamoto N, Osei-Kwasi M, Ofori-Adjei D, and Takaku H. Department of Life and Environmental Science and High Technology Research Center, Chiba Institute of Technology, Chiba-Japan; National Institute of infectious Diseases, AIDS Research Center, Tokyo-Japan; Noguchi Memorial Institute for Medical Research, Department of Virology, Accra-Ghana, and Tokyo Medical and Dental University, Tokyo - Japan

- **PP 2.17** Novel Dimerization Inhibitors acting at the Nanomolar Level : a class of antiproteases to overcome drug resistance in HIV-1 chemotherapy
  Collinet B, Bannwarth L, Boggetto N, Dumond J, Ongeri S, Merabet N, Van Baelinghem L, Sicsic S, Reboud-Ravaux M. Laboratoire d'Enzymologie Moléculaire et Fonctionnelle, Institut Jacques Monod, UMR 7592, CNRS-Universités Paris 6 & 7, Paris, France; Laboratoire de Reconnaissance Moléculaire et Synthèse, Biocis, UMR-CNRS C8076, Faculté de Pharmacie, Université de Paris-Sud, Châtenay-Malabry - France

- **PP 2.18** Sulfonic Acid Polymers as Extracellular HIV-1 Tat and gp120 Proteins Antagonists
  Bugatti A, Urbinati C, Goffi F, Camozzi M, Liekens S, De Clercq E, Presta M, Rusnati M.
  General Pathology and Immunology, Department of Biomedical Sciences and Biotechnology, University of Brescia, Italy. & Rega Institute for Medical Research, Leuven - Belgium

- **PP 2.19** Mutations Conferring Drug-resistance of the Reverse Transcriptase of Human Immunodeficiency Virus Subtype G.
  Garaev MM, Pazilin AS, Shemshura AB, Saukhat SR.
  Institute of Virology, Moscow - Russia

- **PP 2.20** Effects of Antiretroviral Exposure and Genotypic Mutations in Predicting Phenotypic Resistance to Atazanavir (ATV), Lopinavir (LPV), and Tenofovir (TDF) in Patients Naïve to these Drugs.
  Samson P, Rutstein R, Schnittman S, Ortiz A, Graham B, Fenton T, Aldrovandi G, and the Pediatric AIDS Clinical Trials Group P1020A Study Team. Boston, USA

- **PP 2.21** Microbicidal and Virucidal Action of Antioxidants and their Interaction with Iodophores
Hovhannisya HGn. CJSC "Armenicum" Clinical Centre, Yerevan - Armenia

- **PP 2.22** Full Transcriptome Analysis of Genes Altered by HIV in Macrophages
Ottones F, Lejeune M, Manchon L, Piquemal D, Commes T, Marti J. Institut de Génétique Humaine, CNRS UPR 1142, Skuld-Tech, Université Montpellier II, Montpellier - France

- **PP 2.23** Enhanced Degradation of Drug-resistant HIV-1 Reverse Transcriptase is Mediated through Proteasomal Pathway
Starodubova ES, Pazlin AS, Karpov VL, Isaguliants MG. Institute of Molecular Biology, Institute of Virology, Moscow, Russia; Institute of Infectious Diseases, Stockholm - Sweden

- **PP 2.24** Parameter Identification of an HIV/AIDS Dynamical Model
Ouattara DA, Bugnon F, Moog C, Raffi F. IRCCyN (Institut de Recherche en Communication et Cybernétique de Nantes), UMR CNRS 6597, & CHU de Nantes, Centre d'Information et de Soins de l'Immunodéficience humaine, Nantes - France

- **PP 2.25** The Carboxyl-Terminus of HIV-1 Integrase Facilitates Viral Nuclear Import
Cunningham C, Topper M, Muesing MA. Rockefeller University, Aaron Diamond AIDS Research Center, New York - USA

- **PP 2.26** Molecular Homology Between Alpha-defensin And Scrub Typhus Rickettsia Orientia Tsutsugamushi 56kd Type Specific Antigen
Tran MKG, Kirkiacharian S, Maurisson G, Caprani A. University, Paris Sud XI, Faculty Pharmacy, Chatenay Malabry, Centre Medical Europe, University Paris Jussieu, Paris - France

- **PP 2.27** HIV-1 Protease is a Metalloproteinase Containing a Copper-Binding Motif Gly his Lys (GHK) at Residues 68-70
Tran MKG, Kirkiacharian S, Maurisson G, Caprani A, University, Paris Sud XI, Faculty Pharmacy, Chatenay Malabry, Centre Medical Europe, University Paris Jussieu, Paris - France

- **PP 2.28** Incorporation of nucleoside analogs into mitochondrial DNA decreases in the presence of p53 protein.: Bakhanashvili M, Novitsky E, Levy I, Rahav G. Unit of infectious Diseases, Sheba Medical Center, Tel-Hashomer - Israel

- **PP 2.29** High Levels of HIV-1 Infection of CD8 Lymphocytes Expressing CD4 in vivo: Cochrane A, Leen C, Scott G, Simmonds P, University of Edinburgh, Edinburgh - UK

- **PP 2.30** Evaluation of the Abbott LCx HCV-RNA Quantitative Assay: Ceccherini-Nelli L, Malizia T, Giannotti A, Vanni M, Lico S, Avena S, Moriconi F, Comastri G, Pulvirenti FR, Thamm S, Campa M. Dipartimento di Patologia Sperimentale B.M.I.E.,U.O. di Microbiologia Universitaria, AOUP, Pisa, Abbott Molecular Diagnostics, Roma, Italy; Abbott Molecular Diagnostics, Wiesbaden - Germany

- **PP 2.31** Comparison Among Three Different Systems of Genotype Interpretation in HIV Resistance Testing: Setti M, Ventura A, Bruzzone B, Nigro N, Demetri A, Caligiuri P, Cardinale F, Lai P, Department of Internal Medicine, Department of Health Sciences, university of Genoa, Genoa - Italy

- **PP 2.32** Partial Resistance To HIV- 1 Disease Progression Induced By SDF 1 3 ´UTR A 801 G Polymorphism: A Molecular Explanation: Rueda P, García-Moruja C, Torres MC, Alcamí J, Caruz C. Dpto. Biol.
Exp. Universidad de Jaén,Jaén, C.N.B.F. Instituto de Salud Carlos III, Madrid - Spain

- **PP 2.33** Carraguard® Prevents Macrophage Trafficking from Vagina: implications for microbicide development: Perotti ME, Pirovano A, Phillips D. University of Milan, Italy; Population Council, New York - USA

- **PP 2.34** Human Immunodeficiency Virus Transactivator Protein (Tat) Induces a Calcium Increase Through L-type calcium channels of Human Monocytes
Contréras X, Bennasser Y, Chazal N, Moreau M, Leclerc C, Bahraoui E.
Laboratoire d'immuno-virologie, Centre Biologie Développement,
Université Paul SABATIER, Toulouse - France

- **PP 2.35** HIV-1 Tat Directly Binds To NF B Enhancer Sequence: Role In Viral And Cellular Gene Expression
Dandekar DH, Mitra D, Ganesh KN. Organic Chemistry Synthesis, National Chemical Laboratory, National Centre for Cell Science, Pune - India

- **PP 2.36** Molecular Mechanism of Methionine-enkephalin on the Suppression of SIV Infected Lymphocyte Apoptosis
Li P, Liu X, Li G, Xu J. Department of biochemistry and molecular biology, Peking University, Beijing - China

- **PP 2.37** A Rationally Designed CD4 Miniprotein, Useful to Discover Specific Ligands of HIV-1 GP120 Glycoprotein
Stricher F, Martin L, Mechulam A, Mons S, Barthe P, Roumestand C, Ménez A, Veas F, Vita C. Département d'Ingénierie et d'Etudes des Protéines, CEA Saclay, Gif-sur-Yvette, Laboratoire d'Immunologie Rétrovirale et Moléculaire, IRD/CNRS, Centre de Biochimie Structurale, Université de Montpellier, Montpellier - France

- **PP 2.38** Morphine stimulate apoptosis of SIV infected CEM x174 cells
Xu J , Li PF, Liu XH, Li G. Department of biochemistry and molecular biology, Peking University, Heath Science Center, Beijing 100083 - China

- **PP 2.39** Different Characteristics of HCV-specific CD8+ T Cell Responses in Chronic HCV Infection, HIV Coinfection and Spontaneous Clearance
Barrett L, Howley C, Hirsch G, Peltekian K, Bowmer MI, Grant M.
Memorial University of Newfoundland, St. John's, St. John's Health Care Corporation, Dalhousie University, Halifax - Canada

HIV, Clinical Science

- **PP 3.1** The Value of PCR HIV RNA for Early Detection of HIV Infection
Pesic I, Zerjav S. CCS-Institute for Infectious and Tropical Diseases - Virology Department, Belgrade - Serbia & Montenegro

- **PP 3.2** Management of HIV/TB coinfection in Cuba
Díaz Jidy M, González Nuñez I, Pérez Avila J. Institute Pedro Kouri Autopista Novia del Medio Dia, La Haban, Habana - Cuba

- **PP 3.3** BCG skin reaction in Mantoux-negative Healthy Children
Goyal HK,Singla M, Gupta RP. Government Medical College, Patiala - India

- **PP 3.4** Severe Herpes Zoster in Apparently Healthy African Adults: a marker for HIV seropositivity
Onayemi O, Oninla O. A. Department of Dermatology & Venereology, Faculty of Clinical Sciences, Obafemi Awolowo University, Ile-Ife - Nigeria

- **PP 3.5** Acute HCV in a Cohort of HIV-positive Men - Outcomes And Response To Pegylated Interferon-alpha 2b and Ribavirin
Bhagani S, Danta M, Fernandez T, Slapak G, Dusheiko G, Johnson MA.
Royal Free Hospital London - UK

- **PP 3.6** Gynecomastia in an Adolescent with Perinatal HIV Infection: associated variables
  Manfredi R, Calza L, Chiod Fo. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 3.7** 20 years Survey of HIV-related Malignancies in Alsace
  Plaisance N, Lang JM, Beck-Wirth G, Chartier C, Hansmann Y, Michel C, Audhuy B. Hôpitaux Civils de Colmar; Hôpitaux Universitaires de Strasbourg; CH de Mulhouse - France

- **PP 3.8** Acquired Immunodeficiency Syndrome (AIDS) and Multiple Neoplastic Malignancies as Emerging Conditions in the Era of Highly Active Antiretroviral Therapy (HAART)
  Manfredi R, Calza L, Chiodo F.
  Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 3.9** Cardiac Tumor in an HIV-1 Patient
  Comenda E, Cardoso O, Goncalves P, Machado J, Maltez F, Mourao L.
  Hopital de Curry Cabral, Lisboa - Portugal

- **PP 3.10** Vasculitic Neuropathy in HIV Infection
  Minijagap P, Jahathesan K. M.G.R Medical University, Chennai - India

- **PP 3.11** Cognitive Impairement in HIV Patients under HAART : neurophysiological and neurometabolic evaluation
  Poizot-Martin I, Blanquet F, Frixon-Marin V, Michotey P, Drogoul MP, Gastaut JA, Planche D, Vion-Dury J. Service de Neurophysiologie, Hôpital de la Conception, CISIH, Hôpital Ste Marguerite, IRM, Hôpital Ambroise Paré, Service de Neurophysiologie, Hopital de la Timone, et Institut des Neusociences Cognitives de la Méditerranée (INCM, UMR CNRS 6193, Marseille - France

- **PP 3.12** The Epidemiology of the Cryptococcose within the Sick VIH (Hospital point G) in 2002
  Alassane OumarA.A.O , Dao S, Doumbo OK, Diallo M, Diallo A, Poudiougou.
  PB.Faculté Medecine, Pharmacie, Bamako - Mali

- **PP 3.13** Multiple Subcutaneous Lipomas during HIV Disease: which relationship with antiretroviral therapy and dysmetabolism?
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 3.14** Metabolic and Renal Profile before and after Tenofovir DF
  Roca B, Gisbert C, Cabestany B, Perez AP, Ventura JM.
  Hospital General of Castellon - Spain

- **PP 3.15** Cutaneous Drug-reactions associated to Nevirapine: study of risk factors in 101 HIV-positive patients
  Pitche P, Drobacheff-Thiebaut C, Gavignet B, Mercier M, Laurent R. Department of Dermatology, CHU Saint-Jacques, Besançon - France

- **PP 3.16** HIV-HCV Coinfection. Hospital de Navarra (1995-2003)
  Sola J, Gatesi C, Layana E, Castiello J, Reparaz J, Sola I. Servicio Enfermedades Infecciosas, Pamplona - Spain

- **PP 3.17** Study of HIV-infected patients attending an Intensive Care Unit (ICU). Features and prognostic. Comparative analysis between pre- and post HAART eras
  Palacios R, Reina C, Santos J, de la Torre MV, Márquez M.
  Hosp. Virgen de la Victoria. Campus Teatinus, Málaga - Spain

- **PP 3.18** Fulminating Lactic Acidosis in a Woman with Disseminated Tuberculosis and Advanced HIV in the Absence of anti-retroviral Therapy
  Marshall BG, Rowen D, Addis B. Southampton University Hospitals NHS Trust Tremona Road, Southampton, SO16 6YD, Hampshire - UK

- **PP 3.19** Increasing AIDS ¯Presenters: a further concern of the Highly Active Antiretroviral Therapy (HAART) Era
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 3.20** The potential of volumetric flow cytometry to follow up CD4 of HIV/AIDS patients in resource poor settings
  Göhde W, Cassens U, Greve B. Institute of Radiobiology, Institute of Transfusion Medicine, University Hospital, Münster - Germany

- **PP 3.21** HIV-Associated Psychiatric Disorders
  Farazi E. Mashad University of Medicine - Iran

- **PP 3.22** Management of hyperlactatemia in three HIV-positive patients assuming ART
  Moretti F, Quiros-Roldan E, Prestini K, Torti C, Casari S, Carosi G. Department of Infectious and Tropical Diseases, University of Brescia, Brescia - Italy

- **PP 3.23** Malabsorption and Septicaemia: Association in and Implications for Children in an Area of High HIV Prevalence : Chhagan MK, Kauchali S. University of KwaZulu-Natal, Nelson R Mandela School of Medicine, Durban - South Africa

- **PP 3.24** The Evolution of Surgical Practice in HIV/AIDS - A 16 years experience
  Dua S, Wajed S, Winslet M.
  University Dept of Surgery, Royal Free Hospital, Pond Street, London NW3

- **PP 3.25** ARVs Side Effects Leads To Poor Compliance Hence Resistance
  Byaruhanga BR, Mugyenyi MP, Kityo KC, Otim OT, Mwebesa MD. Joint Clinical Research Center, Kampala - Uganda

HIV, Therapy

- **PP 4.1** TMC114/RTV Activity in PI-experienced Patients: correlations of baseline genotype, phenotype, PK and IQ with antiviral activity at day 14
  Peeters M, Van Baelen B, De Meyer S, de Bethune MP, Muller H, Hoetelmans R, Lefebvre E. Tibotec Inc., Yardley, USA; Tibotec, Mechelen - Belgium

- **PP 4.2** Impact of the Adverse Effects of HAART in Various Clinical Situations on the 3/5 Initiative of WHO-resource Limited Country Setting: a pilot study
  Ketha P. State Nodal Officer for the Control of AIDS, Project Implementation Plan, Phase II, National AIDS Control Organisation, Andhra Pradesh -India

- **PP 4.3** Care and Treatment Issues of PLWHAs in Resource Poor Conditions
  Agrawal R & Ghosh P. Bhoruka Public Welfare Trust, Kolkata - India

- **PP 4.4** Scaling up Antiretroviral Therapy in Jamaican Children
  Evans-Gilbert T, Pierre R, Steele -Duncan J, Rodriguez B, Whorms S, Figueroa, PJ, Christie CDC. Bustamante Hospital for Children Kingston - Jamaica

- **PP 4.5** About Early Atazanavir Availability In France
  Vivona V, Vincentelli J, Drogoul MP, Marimoutou C, Poizot Martin I, Penot Ragon C, Gastaut JA.
  Pharmacie Hôpital, CISIH-SUD Unité d'Hématologie-VIH Hôpital Sainte Marguerite, Marseille - France

- **PP 4.6** Prise en Charge Communautaire des PVVIH Soins de Santé de Base à Domicile par les Jeunes Volontaires en Lutte contre le SIDA (AJVLS) : visite à domicile dans Lomé-Commune (TOGO)
  Association des Jeunes Volontaires en Lutte contre le SIDA (AJVLS), Lome - Togo

- **PP 4.7** Close Collaboration between Physician and Virologist for a Stage CDC-3 AIDS Patient : importance of genotype assessment for the choice of efficient antiretroviral therapy
  Dulioust A, Naudin CA, Cottreau D, Jauneau M. Centre Médical de Bligny, Briis/forges - France

- **PP 4.8** High Prevalence of Nephrolithiasis in HIV- infected Patients Co-infected with Hepatitis C Virus Treated with Indinavir+Ritonavir
  Dragovic G, Jevtovic Dj. Institute of Clinical Pharmacology; Pharmacology and Toxicology, School of Medicine, University of Belgrade, Belgrade; Institute of Infective and Tropical Disease - HIV/AIDS Unit - School of Medicine, University of Belgrade, Belgrade - Serbia & Montenegro

- **PP 4.9** The Phenomenon of HIV-infected Patients taking only Isolated Dual Nucleoside Analogue Antiretroviral Therapy, Eight Years after HAART Introduction. Practical issues and concerns
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 4.10** Impact of the HCV Co-infection in Naïve HIV-1 Infected Patients Treated with HAART
  Silva S, Ferreira A, Tavares M, Piñeiro C, Xerinda S, Serrão R, Diaz-Brito V, Marques R, Mota Miranda A. Infectious Diseases Department, Hospital S. Joao & School of Medicine, Porto - Portugal

- **PP 4.11** Nelfinavir in HCV - HIV coinfected patients: 24 Months' follow up
  Poizot-Martin I, Marimoutou C, Drogoul-Vey MP, Vion-Dury F, Frixon-Marin V, Benhaim S, Poggi P, Gastaut JA. CISIH-SUD- Hematology- HIV Unit, Clinical Research Department Sainte-Marguerite Hospital, CHU of Marseilles - France

- **PP 4.12** Predictive Factors for Saquinavir-ritonavir combination (SQV/r) Efficacy in Real Life
  Tissot-Dupont H, Mars-Kallee ME, Montestruc F, Tomeï C, Martin S, Lecomte V, Gallais H. La Conception Hospital, Marseille, France; Roche Laboratories, Neuilly - France

- **PP 4.13** Saquinavir-ritonavir Baby Dose Combination (SQV/r) : Same efficacy and better tolerance in real life than Saquinavir-Ritonavir high dose (SQV/R)
  Tissot-Dupont H, Mars-Kallee ME, Montestruc F, Tomeï C, Martin S, Lecomte V, Gallais H. La Conception Hospital, Marseille, France; Roche Laboratories, Neuilly-sur-Seine - France

- **PP 4.14** Influence du Passage à l'Association Lamivudine, Zidovudine, Abacavir (TRIZIVIR) sur l'Observance des Traitements Antirétroviraux.
  Jouglen J, Clement F, Minot A, Lacoste D, Pometan JP. Service Pharmacie, Service de médecine interne, CHU de Bordeaux, Hôpital Saint-André, Bordeaux - France

- **PP 4.15** Relevance of Lopinavir/r Therapy in Heavily pre-treated Patients
  Sola J, Layana E, Alaez JI, Sola I, Uriz J, Castiello J, Reparaz J. Clinico Universitario, Madrid - Spain

- **PP 4.16** Metabolic Evaluation of Kaletra (LPV/r)-containing Regimens
  Lafeuillade A, Hittinger G, Geoffroy M, Poggi C, Delbeke E, Jolly P, Lambry V, Philip G. General Hospital, Toulon - France

- **PP 4.17** Antiretroviral Usage in a Large Metropolitan Area of Northern Italy. Selected drugs and related costs
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 4.18** A Comparison of the Two First-line Recommended Antiretroviral Regimens for Naïve HIV-infected Subjects
  Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 4.19** Advances in Antiretroviral Therapy of HIV Infection
  Akomiah P, Bio T, University of Cape Coast, Cape Coast - Ghana

- **PP 4.20** Interruption Thérapeutique Progammée chez l'Enfant Infecté par VIH.
  Monpoux F., Tricoire J., Lalande M, Reliquet V, Thuret I. CHU de Nice, Toulouse, Montpellier, Nantes, Marseille - France

- **PP 4.21** Efficacy Evaluation of Combined Chemoprophylaxis of Vertical HIV Transmission
  Shostakovich-Koretskaya LR, Hozhilo II, Chykarenko ZA, Cherginets AV. Dniepropetrovsk State Medical Academy, Dniepropetrovsk - Ukraine

- **PP 4.22** A Pilot Study Evaluating the Efficacy and Safety of a Bioadhesive Buccal Tablet of Miconazole 50 mg (Miconazole LauriadTM) in HIV Positive Patients with Oropharyngeal Candidiasis
  Dupont B, Dellamonica P, Datry A, Consigny PH, Kirstetter M, Poizot-Martin I, Meyohas MC, Chaumont C, Croughs T, Lafeuillade A. Hosp Necker, Hosp Pitié Salpêtrière, Hosp Bichat, Private institution, Hosp Saint Antoine, BioAlliance Pharma, Paris; Hosp Archet. Nice; Hosp Sainte Marguerite, Marseille; Hosp Chalucet, Toulon - France

- **PP 4.23** Algorithmic Guidelines in the Management of Dysphagia and Odynophagia in Immune-compromised Patients at Kigali University Hospital
  Murenzi FC, Van Den Ende J. National University Of Rwanda, Kigali - Rwanda

- **PP 4.24** Filling Treatment of Facial Lipoatrophies by a Biodegradable Product in HIV Patients
  Carbonnel E, Claudy A. Hopital E. Herriot, Lyon - France

- **PP 4.25** Use of Pyrimethamine-Sulfadoxin in Treatment of Cerebral Toxoplasmosis in HIV Infected Patients
  Gomez JE, Alvarado F, Hernandez C, Cuervo S, Saravia J. Centro Investigaciones bio medicas, Universidad del Quindio - Colombia

- **PP 4.26** Therapeutic Drug Monitoring (TDM) of Nelfinavir (NFV): Recommendations for Optimization
  Laurent S, Sigrist H, Solas C, Poizot-Martin I, Chadapaud S, Frixon-Marin V, Lafeuillade A, Dhiver C, Moreau J, Pichancourt G, Ravaux I, Cohen Valensi R, Ruer J, Lacarelle B.Timone Hospital, Sainte-Marguerite Hospital, Conception Hospital, Nord Hospital, Marseille; Chalucet Hospital, Toulon; Henri Duffaut Hospital, Avignon; Martigues Hospital, Martigues - France

- **PP 4.27** How a Warning can Avoid a Medicine Error
  Boivin H, Nau P, Andre V, Rouleau A. Pharmacy CHRU Tours, - Hospital Bretonneau - France

- **PP 4.28** Comparison of Efficacy of Two Interventions to Enhance Adherence to Antiretroviral Therapy (HAART)
  J. Benkimoun J, Gnamien S, Dupont C, Chaltiel L, Aubry N, Le Mercier F, Rouveix E, Lebas-Certain M. Department of Pharmacy & Department of Internal Medicine, Hôpital Ambroise Paré (AP-HP), Boulogne - France

- **PP 4.29** Cultural Adaptation and Validation of a Lipodystrophy Quality of Life Questionnaire
Duracinsky M, Cervoni J, Vincent V, Lascoux C, Sereni D, Molina JM, Acquadro C, Wu A, Chassany O. Hôpital de Bicêtre; Hôpital Lariboisière, Hôpital Saint-Louis, Paris; MAPI Research Institute, Lyon, France; Johns Hopkins University, Baltimore - USA

- **PP 4.30** Persistent Low Viremia and Future Treatment Options
Dyner T, Cafaro V, Chow V. Shared Perspectives on Therapies, San Francisco - USA

- **PP 4.31** Impact of Highly Active Antiretroviral Therapy (HAART) on Blood Pressure (BP) in Patients with HIV Infection. A prospective study in a cohort of naïve patients
Palacios R, Santos J, Castell E, González M, Ruiz J, Márquez M. Hosp Virgen de la Victoria. Campus Teatinus, Málaga - Spain

- **PP 4.32** HIV Positive Patients' Perspectives about their Adherence to Antiretroviral Therapy
Morillo García A., Gasch Illescas A., Valencia Martín R., Aldana Espinal JM, Conde Herrera M. Virgen del Rocío Hospital, 41013 Sevilla - Spain

- **PP 4.33** Patients-reported Factors Influencing Adherence to Antiretroviral Therapy
Montana M, Darque A, Ravaux I, Gallais H, Gensollen S, Bongrand MC, Timon-David P. Hospital Pharmacy, Infectious Diseases Wards, Conception Hospital, Marseille - France

- **PP 4.34** Antiretroviral Prescriptions Proved Significant Different Between the Two Outpatient Centres of a Metropolitan Area in Northern Italy: An Analysis of Economic Correlates
Manfredi R, Calza L, Chiodo F. Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 4.35** Comparison of Toxicity and the Dyslipidemic profile of the Two Available non-nucleoside Reverse Transcriptase Inhibitors: significant differences between Nevirapine and Efavirenz Manfredi R, Calza L, Chiodo F.
Infectious Diseases, University of Bologna, S. Orsola Hospital, Bologna - Italy

- **PP 4.36** Glycyrrhizin Production from Transformed Licorice Cells
Kovalenko P.G., Maliuta S.S. Institut of Molecular biology and genetics NASU, Zabolotnogo, Kiev -Ukraine

- **PP 4.37** Efficacy of Enfuvirtide in Patients Infected with a Drug-resistant Human Immunodeficiency Virus (HIV-1)
Lebaudy C, Ghnassia C, Poinsignon Y. Vannes Hospital - France

- **PP 4.38** Natural Treatment for HIV/AIDS
Schelonka EP. Good News Medical Clinic, Belize City, Belize - Central America

- **PP 4.39** Vivre avec le Secret du VIH et des Multithérapies pour un Groupe de Femmes Montréalaises
Trottier G, Massie L, Toupin I, Fernet M, Otis J, Pelletier R, Bastien R, Josy Lévy J, Samson J, Boucher M, Lapointe N, Harerimana M et Rateau M. Québec - Canada

- **PP 4.40** Two-drug ART in Treatment Naïve HIV-infected Persons in Resource-limited Setting: 2-year study
Yanamadala VMKR. Association of People Against AIDS, Kakinada, Andhra Pradesh - India

- **PP 4.41** The Dissociation Between Immunologic and Virologic Response to HAART
Pesic I, Salemovic D, Ranin J, Zerjav S, Jevtovic Dj. The Institute of Infectious and Tropical Diseases, Belgrade - Serbia & Montenegro

- **PP 4.42** Utilization of HIV Post Exposure Prophylaxis Among Health Care Workers in Selected Health Institutions In Nairobi
Maina JW, Wasunna MK, Orago AS, Okelo RO.Kenyatta University, Nairobi - Kenya

- **PP 4.43** High Thymic Volume and Output at Baseline is Associated to Enhancement of Viral Replication and Immunologic Impairment Early after HAART Discontinuation in Chronic HIV Infection
Vallejo A, Valladares A, De Felipe F, Vivancos J, Soriano-Sarabia N, Gutierrez S, Molina-Pinelo S, Ruiz-Mateos E, Lissen E, Leal M. Hospital Virgen del Rocio, Seville - Spain

- **PP 4.44** The Benefit of the Combination Antiretroviral Therapy (ART) for the Treatment of HIV Infected Patients in Slovakia
Habekova M, Stanekova D, Mokrá M. Slovak Health University - Institute of Preventive and Clinical Medicine, Department of Geographical and Infectious Medicine of Derer Hospital, Bratislava - Slovakia

- **PP 4.45** Virologic Efficacy and Pharmacokinetic of Saquinavir/Ritonavir Baby Dose once Daily (QD) combination in PI (protease inhibitor) Pretreated HIV-1 + Patients: Brunel-Dalmas F, Livrozet JM, Gagnieu MC, Bru JP, Michon C, Touraine JL. Hôpital E. Herriot, Lyon, Hôpital d' Annecy, Roche, Neuilly-sur-Seine - France

- **PP 4.46** Early HCV-RNA Kinetic In HIV Patients With Chronic Hepatitis C Treated With PEG-IFN Alpha-2a And Ribavirin: Setti M, Blanchi S, Basso M, Sticchi C, Pelli N, Murdaca G, Indiveri F, Picciotto A. Department of Internal Medicine, Department of Health Sciences, University of Genoa, Genoa - Italy

- **PP 4.47** Nanoparticles Associated to Zidovudine as an Innovative Approach for Targeting Intestinal Reservoir During HIV Infection: Dembri A, Soursac M,Thomas CM, Maquin A, Cheret A, Ponchel PG, Constantini D. Bioalliance pharma, Paris, Laboratoire de Pharmacie Galénique, Université Paris XI, Châtenay-Malabry - France

- **PP 4.48** Higher Risk of Antimalarial Treatment Failure in HIV Positive than in HIV Negative Individuals with Clinical Malaria: Van Geertruyden JP, Mwananyanda L, Chalwe V, Mwanakasale V, Moerman F, Chilengi R, Kestens L, D'Alessandro U. Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium; Tropical Diseases Research Centre, Ndola - Zambia

- **PP 4.49** Inhibitor Design for Drug-Resistant Forms of Aspartic Protease of HIV: Frecer V, Miertus S. International Centre for Science and High Technology, UNIDO, AREA Science Park, Trieste - Italy

- **PP 4.50** Efficacy of Enfuvirtide (FUZEON®) in HIV1-Infected Patients with Failure or Intolerance to Antiretroviral Treatment:Faye F, Darque A, Ravaux I, Gallais H, Gensollen S,Timon-David P, Bongrand MC. Pharmacy, Public Hospital System Conception, Infectious diseases ward, Marseille - France

- **PP 4.51** PC-815, a Novel Combination Microbicide:Romero JF, Thorn M, Phillips D. Population Council, New York - USA

- **PP 4.52** Lack of an Effect of Atazanavir on Steady-State Pharmacokinetics of Methadone in Chronically Treated Subjects
Friedland G, AndrewsL, Agarwala S, Schreibman T, Daley L, Child M, Wang Y, O'Mara E. Yale School of Medicine, New Haven, CT; Bristol-Myers Squibb, Princeton, NJ, USA

- **PP 4.53** Follow Up of the Resistance Mutations Archives During Genotype Guided HAART
Parisi SG, Mazzi R, Gatti F, Carolo G, Nicastri E, Concia E, Dal Bello F, Montano M, Palù G, Andreoni M. Microbiology Dept, Padua Hospital, Padua, Public Health Dept, Tor Vergata University, Rome, Infectious Diseases Dept, Verona Hospital Verona - Italy

- **PP 4.54** Long Term Immunological Benefit with Double Nucleoside Therapy : Genotype Markers
Parisi SG, Mazzi R, Sarmati L, Gatti F, Carolo G, Concia E, Montano M, Dal Bello F, Palù G, Andreoni M. Microbiology Dept, Padua Hospital, Padua, Public Health Dept, Tor Vergata University, Rome, Infectious Diseases Dept, Verona Hospital Verona - Italy

- **PP 4.55** HIV-1 Drug Resistance Among Tunisian Subjects With Therapeutic Failure
  Jlizi A, Ben Halima M, Slim A, Tebourski F, El Gaaied A, Ben Chaabane T, Chakroun M, Letaief-Ommezinz A, Garbouj M. Laboratoire de Microbiologie, Hôpital Charles Nicolle, Laboratoire de Génétique Moléculaire, Immunologie et Biotechnologie, Faculté des Sciences, Service de Pathologie Infectieuse, Hôpital La Rabta, DSSB, Ministère de la Santé Publique, Tunis, Service de Pathologie Infectieuse, Hôpital Fattouma Bourguiba, Monastir, Service de Pathologie Infectieuse, Hôpital Farhat Hached, Sousse - Tunisia

- **PP 4.56** Relative Quantification of Human Immunodeficiency Virus type 1 proviral DNA in Patients undergoing Structured Treatment Interruption
  Kabamba-Mukadi B, Henrivaux P, Ruelle J, Bodeus M and Goubau P.
  Université Catholique de Louvain, Bruxelles, Service de Médecine interne, Clinique Saint Joseph, Liège - Belgium.

- **PP 4.57** Safety Assessment of Patients Receiving Atazanavir (ATV) With Ritonavir (RTV), ATV With Saquinavir (SQV), or Lopinavir (LPV)/RTV: 48-Week Results From BMS AI424-045: Clotet B, Lazzarin A, Grinsztejn B, Lichtenstein K, Sankoh S and Wilber R. IrsiCaixa Foundation, Barcelona, Spain; S. Raffaele Hospital, Milan, Italy; Instituto de Pesquisa Clínica Evandro Chagas-Fiocruz, Rio de Janeiro, Brazil; University of Colorado Health Sciences, Denver, CO; Bristol-Myers Squibb, Wallingford, CT, USA

HIV, Immunology & Vaccines

- **PP 5.1** CRF01_AE (subtype E) Gag Specific T-lymphocyte Responses In HIV-Infected Individuals Differ From That In Highly Exposed But HIV-Seronegative Individuals In Thailand
  Sriwanthana B, Jitjuk B, Wichukchinda N, Rojanawiwat A, Tanaka M, Pathipvanich P, Ariyoshi K, Sawanpanyalert P. National Institute of Health, Nonthaburi, Lampang Hospital, Lampang, Thailand

- **PP 5.2** Effects of Exogenous Nef Protein on Immune System
  Pugliese A, Petrini S, Beltramo T, De Checchi S, Gallo G & Vidotto V. Department of Medical and Surgical Sciences, Section of Clinical Microbiology of Turin University, "Amedeo di Savoia" Hospital, Turin - Italy

- **PP 5.3** Construction of Candidate DNA-Vaccines against HIV
  Babkina IN, Pozdnyakov SG, Ryazankin IA, Babkin IV, Shchelkunov S. State Research Center of Virology and Biotechnology "Vector", Koltsovo, Novosibirsk region - Russia

- **PP 5.4** Poly-CTL Epitope Immunogen, Candidate for DNA-vaccine against HIV-1
  Bazhan SI, Belavin PA, Seregin SV, Danilyuk NK, Babkina IK, Karpenko LI, Nekrasova NA, Lebedev LR, Ignatyev GM, Agafonov AP, Ilyichev AA. SRC VB Vector; Koltsovo, Novosibirsk Region - Russia

- **PP 5.5** Mimotopes of Human Immunodeficiency Virus Type 1 Diagnostic and Neutralizing Envelope Epitopes
  Gazarian K, Palacios Y, Gazarian T, Mailuf A. Mexican Nacional Autonomous University, Mexico City, Mexico; Regional Hospital Gabriel Mancera, Mexico City - Mexico

- **PP 5.6** Different Delivery Systems for Artificial Polyepitope HIV-1 Antigen: Nekrasova N A, Ignatyev G M, Agafonov AP, Lebedev LR, Ilyichev A A, Karpenko LI. The State Research Center of Virology and Biotechnology "VECTOR" Koltsovo, Novosibirsk Region - Russia

- **PP 5.7** Effects of Poly-glycine Linker on the Presentation of the Foreign Epitopes : Shahrokhi N, Bouzari S, Jafari A. Pasteur Institute of Iran, Tehran - Iran

- **PP 5.8** Chimeric Core Particles HBcAg Carrying Epitopes from Pres Region of HBV Surface Protein
  Veremeiko TA, Lebedev LR, Zaitsev BN, Nekrasova NA, Ilyichev AA, Karpenko LI
  The State Research Center of Virology and Biotechnology "VECTOR" Koltsovo, Novosibirsk Region - Russia

Emerging Infectious Diseases

- **PP 6.1** Helinx Technology Inactivates High Titers of SARS-CoV, WNV and Vaccinia in Platelet Concentrates
  Dupuis K, Sampson-Johannes A, Bernard K, Sawyer L. Cerus Corporation, Concord, CA; New York State Dept. of Health, Slingerland, NY - USA

- **PP 6.2** Chinese Herbal Medicine for Severe Acute Respiratory Syndrome (SARS): a Systematic Review and Meta-Analysis
  Liu JP, Manheimer E, Shi Y, Gluud C. Liverpool School of Tropical Medicine Liverpool, UK ; University of Maryland School of Medicine, Baltimore, USA; Shanghai University of Traditional Chinese Medicine, Shanghai, China; Copenhagen University, Copenhagen - Denmark

- **PP 6.3** Mucosal Immunogenicity of Surface-displayed SARS Viral Antigens on Lactic Acid Bacteria
  Kim CJ, Lee JS, Poo H, Sung MH. College of Veterinary Medicine, Chungnam National University, Bioleaders Corp., Korea Research Institute of Bioscience and Biotechnology, Daejeon, Korea - South

- **PP 6.4** The Role of TT Virus (TTV) Infection in Human Pathology - The Analysis of Observed Cases
  Tomasiewicz K, Modrzewska R, Krawczuk G, Łyczak A. Department of Infectious Diseases Medical University of Lublin - Poland

- **PP 6.5** Out of Africa: A Sorry Safari
  Uslan DZ, MD and Sia IG. Mayo Clinic, Rochester MN - USA

- **PP 6.6** Association of a Novel Perforin Gene Polymorphism with HTLV-I Infection in Mashhad, North East of Iran
  Farid R, Kharazmi A, Nobahar V. Mashhad University of Medical Sciences, Mashhad - Iran

- **PP 6.7** Clinical Profile of Dengue Outbreak in Delhi
  Bhoi S, Kheira A, Wasir J. All India Institute of Medical Sciences, New Delhi - India

- **PP 6.8** Comparison of HCV RNA and HCV Core Antigen Kinetics in the Follow-up of a Therapeutic Protocol in HCV-HIV Coinfected Patients (RIBAVIC)
  Lunel F, Pivert A, Payan C, Morand P, and the members of the Ribavic Scientific Committee (ANRS HC02). Laboratoire de Bactériologie-Virologie, CHU Angers, France ; Laboratoire de Virologie, CHU Grenoble - France

- **PP 6.9** Prophylactic and Therapeutic Effects of Small Interfering RNA Targeting SARS-Coronavirus
  Zheng Bj, Guan Y, Tang Q, Cheng D, Xie FY, He ML, Chan KW, Wong KL, Lader E, Woodle MC, Lu PY, Li B, Zhong N. Department of Microbiology, Institute of Molecular Biology, Department of Pathology, University of Hong Kong, Hong Kong - China

- **PP 6.10** An Exceptional Case Report of Very Early Tertiary Syphilis in a Young Adult
  Manfredi S, Sabbatani S, Chiodo F. Infectious Diseases, University of Bologna, Bologna - Italy

- **PP 6.11** Favorable Long-term Management of a HIV-unrelated Brain Cryptococcoma with Voriconazole, after Fluconazole Failure
  Manfredi R, Sabbatani S, Pavoni M, Consales A, Chiodo F. Infectious Diseases, University of Bologna, and 1Department of Neurosurgery, Bellaria Hospital, Bologna - Italy

- **PP 6.12** Clinical and Microbiological Features of Capnocytophaga spp. As an Emerging Pathogen in Brain Abscess
  Manfredi R, Sabbatani S, Frank G, Chiodo F. Infectious Diseases, University of Bologna, and Department of Neurosurgery, Bellaria Hospital, Bologna - Italy

- **PP 6.13** Emerging Severe Central Nervous System Infections, and Potential Role of Linezolid Administration in Three Different Clinical-microbiological Scenarios
  Manfredi R, Sabbatani S, Frank G, Chiodo F. Infectious Diseases, University of Bologna, and Department of Neurosurgery, Bellaria Hospital, Bologna - Italy

- **PP 6.14** Cat-Scratch Disease as an Emerging Illness in both Children and Adults: Clinical Presentation and Management Perspectives
  Manfredi R, Sabbatani S, Chiodo F. Infectious Diseases, University of Bologna - Italy

- **PP 6.15** Diarrhea Caused by New Organisms
  Kwaabena Appau G, Kofi Owusu K. Institute of Advanced Technology, Kumasi - Ghana

- **PP 6.16** The Evaluation of Antibacterial Pattern of Nosocomial Pathogens Isolated in Iran
  Khorshidi A, Sharif A, Moosavi GH. Kashan University of Medical Sciences, Kashan, Iran

- **PP 6.17** Evaluation of Acute Bacterial Sinusitis Etiology and Determination of Antibiotic Sensivity in Iran
  Khorshidi A, Yeganeh Moghaddam A, Sokoot A, Moosavi GH. Kashan University of Medical Sciences, Kashan - Iran

- **PP 6.18** Clinical Finding in Patient Presenting with Sore Throat.
  Khorshidi A, Taghaddosi M, Nadi Ravandi M, Hosseini nejad A, Khorshidi S. Kashan University of Medical Sciences, Kashan - Iran

- **PP 6.19** Prevalence of Neisseria gonorrhoeae in Cervicitis and Evaluation of Drug Resistance of Neisseria gonorrhoeae in Kashan-Iran
  Tabassi A, Khorshidi A, Alinaghi N. Kashan University of Medical Sciences, Kashan - Iran

- **PP 6.20** Embryonic Hematopoietic Stem Cells in Chronic Active Hepatitis
  Smikodub OI. Cell Therapy Clinic of National Medical University and Embryonic Tissues Center EmCell, Kiev - Ukraine

- **PP 6.21** Significantly Increased Frequency of Hepatitis A in a Metropolitan Area of Northern Italy. Need of Counselling and Prophylactic Measures for Male Homo-bisexual Population
  Manfredi R, Sabbatani S, Frank G, Chiodo F. Infectious Diseases, University of Bologna, and Department of Neurosurgery, Bellaria Hospital, Bologna - Italy

- **PP 6.22** A Standardized Infectious Disease Screening of Patients Undergoing Orthotopic Liver Transplantation
  Manfredi R, Sabbatani S, Frank G, Chiodo F. Infectious Diseases, University of Bologna, and Department of Neurosurgery, Bellaria Hospital, Bologna - Italy

- **PP 6.23** Myxobolus sp., a Possible New Opportunistic Parasite in Immunocompromized Patients
  Hessen EM, Zamzame ML. Faculty of Medicine, Suez Canal University, Ismailia - Egypt

- **PP 6.24** Helicobacter pylori Infection in Children: Utility of Culture in Diagnosis and to Study the Anti Microbial Susceptibility
  Sabbi T, Argentieri M, Menichella D, De Angelis P, Torroni F, Federici di Abriola G, Colistro F, Dall'Oglio L. Pediatric Unit Belcolle Hospital, Viterbo; Microbiology Department, Digestive Surgery and Endoscopic Unit, Biochemistry Bambino Gesù Pediatic Hospital - Rome

- **PP 6.25** Incidence Of Chlamydia Trachomatis In Genital Infections
  Kovov D, Kovova N, Parmuzina R. Vitebsk State Medical University, Vitebsk - Belarus

- **PP 6.26** Purification Of Trichomonad DNase By DNA-cellulose Affinity Chromatography
  Mathur HSS, Perry D, Greenwell P. University of Westminster, London - UK

- **PP 6.27** Molecular Characterisation of Enterotoxigenic Escherichia coli Isolates from Children with Diarrhoea
  Jafari A, Bouzari S. Pasteur Institute of Iran, Tehran - Iran

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OP 1.1.
Recent Data on HIV Resistance to Antiretroviral Drugs

No abstract available

OP 1.2.
Resistance to RT Inhibitors

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Considerable progress has been made in defining the indications for resistance testing and determining the cost-effectiveness of strategies that use testing in the management of HIV-infected individuals. Prospective randomized trials have shown at least short-term virological benefits for both genotypic and phenotypic resistance testing in a variety of situations. Moreover, emerging data indicate that viral drug resistance is a problem wherever treatment is used, and it may be increasing in importance. It has also become clear that knowledge concerning patterns of resistance and cross-resistance is critical to the development of successful sequencing of antiretroviral regimens.

The specific mechanisms of nucleoside reverse transcriptase inhibitor (NRTI) resistance are now better understand, as well as the observed levels of resistance associated with the various patterns of mutations encountered in clinical practice.

Two distinct resistance pathways toward NRTI emerged. Some reverse transcriptase mutations lead to an enhanced excision of the analogue from the nascent DNA strand; other mutations reduce the incorporation efficiency of the nucleotide triphosphate form of the NRTI.

The removal of the chain-terminator after it has been incorporated into the growing chain can occur in one of two mechanisms. In one mechanism, the pyrophosphate reacts in the presence of mutations to facilitate removal of the chain terminator and take it out of the growing chain. This opens up a site for substrate to come in and carry on growth, and the virus escapes inhibition. The second mechanism involves a process when NTP acts as a donor to remove the chain terminator. Instead of pyrophosphate being released when the nucleoside analogue triphosphate is incorporated into the viral DNA chain, the presence of multiple resistance mutations in reverse transcriptase prevents translocation and allows removal of the nucleoside analogue. The extension process can then proceed by the addition of a cellular nucleoside building block.

This mechanism of resistance within reverse transcriptase concerns the mutations selected by zidovudine (41L, 67N, 70R, 210W, 215Y/F, and 219E/Q) that tend to accumulate during continued exposure to zidovudine in the absence of good viral suppression. Recently, it has been appreciated that these mutations can also be selected by stavudine, and that they have implications for resistance to all drugs in the NRTI class and to the recently FDA-approved nucleotide reverse transcriptase inhibitor, tenofovir. Thus, these mutations are probably best referred to as nucleoside analogue mutations (NAMs), since they can affect the entire class.

The other NRTI resistance pathway that occurs through the efficiency of discrimination concerns mainly single point mutations, like M184V, K65R and L74V.

The 184V mutation that can result in up to 1000-fold increases in resistance to lamivudine also appears to interact with NAMs to modulate resistance to all the other NRTIs. In reverse transcriptase that contains no more than 2 or 3 NAMs, this mutation enhances translocation during reverse transcription, decreasing excision of the nucleoside analogue residue. However, as the number of NAMs increases, 184V does not have enough effect to prevent excision.

The take-home message is that NAMs are bad for this class of antiretrovirals, and the accumulation of high numbers of these mutations should be assiduously avoided. Thus, viral load and resistance monitoring should be used together to ensure that therapy is changed before high numbers of NAMs evolve. The appearance of the 184V mutation may improve sensitivity to many of the drugs in this class, but it will not "reverse" high-level resistance. Nonetheless, inclusion of lamivudine in salvage regimens may improve the effectiveness of the NRTI components of therapy, and it is certainly a well-tolerated drug – an important issue for most patients receiving salvage therapy.

In conclusion, the critical problem in the clinical setting is that a mutant selected for by a failing regimen may have some degree of cross-resistance to other drugs in the same class that have not yet been prescribed to that patient. The development of cross-resistance may lead to a reduced virologic or immunologic response to subsequent regimens. As scientists develop new agents active against resistant virus, clinical medicine is also implementing diagnostic strategies designed to detect antiretroviral resistance and individualize subsequent regimens.

OP 1.3.
Gestion des Résistances croisées (RC) aux Inhibiteurs de Protéase (IP), le point de vue du clinicien

Denis Lacoste, Bordeaux - France

Ce n'est pas heureusement encore le problème des résistances primaires peu fréquentes sauf cas particuliers, mais c'est un des challenges d'aujourd'hui que de ne pas compromettre l'avenir thérapeutique des patients en ciblant les premières lignes thérapeutiques de façon à ne pas risquer de voir apparaître de mutations barrant la route aux IP en seconde intention.

S'informer et se former est ici plus que jamais devenu indispensable, ainsi que maintenir son niveau de connaissance.
Les échanges entre cliniciens, virologues, pharmacologues sont désormais la clé de la qualité de prise en charge des patients nécessitant un traitement anti-rétroviral (ARV).

La communauté scientifique est de plus en plus convaincue de la nécessaire prise en compte de l'archivage des mutations dans l'histoire thérapeutique des patients, déterminant les choix d'associations d'ARV.

Les recommandations nationales sont de bons guides à priori mais l'analyse au cas par cas reste la plus part du temps souhaitable.

Prévenir les RC fait partie du quotidien
- Soit en première intention, par l'épargne des IP, ou si un schéma avec IP est recommandé, faire le bon choix adapté au contexte.
- Soit en seconde intention ou en nième ligne de traitement, savoir corriger les choix avec l'aide d'algorithmes à jour, se faire aider des avis spécialisés comme cela est dit plus haut; des choix comme l'utilisation d'autres classes d'ARV, l'interruption thérapeutique seront discutés.

Des IP " Stars " apparaissent en terme de mutagénèse et/ou de simplification thérapeutique… Doit-on toujours céder aux sirènes ?

Enfin, que dire des possibilités restreintes de certains pays où l'avenir est en train de se jouer au fil des mises à disposition parfois anarchiques de tel ou tel IP ?

OP 1.4.
Resistance & Reservoirs

No abstract available

OP 1.5.
Rational Prescribing in the Era of HIV Phenotypic Drug Resistance Testing

G. Hess, C. Nelson, N. Lipskiy
Surveillance Data, Plymouth Meeting PA USA

Objective: In the U.S. patients newly diagnosed with HIV infection are generally treated initially with three-drug regimens. Although guidelines have emerged encouraging the use of resistance testing to help guide therapy, access and insurance coverage for the service varies across the US. In addition, while average resistance on a national level may be known, there may be regional differences. Clinicians prescribing decisions may also be influenced by considerations beyond reduced susceptibility i.e. resistance. We studied and compared phenotypic resistance and antiviral prescribing trends by different regions in the U.S during July 2002 to June 2003, the HAART era.

Methods: An automated sample of patient-level phenotypic resistance testing data from Virologic Inc. was retrospectively analyzed for July 2002-June 2003. Test results were mapped to their respective zip codes. Antiviral retail prescription data covering approximately 65% of the U.S. population was analyzed for the same period and geographies. Phenotypic resistance by class and antiviral prescribing by class (NNRTI, NRTI and PI) was compared for each of the four U.S. census regions. Results were analyzed using regression and descriptive statistics for significant differences.

Results: There were approximately 22,000 patient specimens tested against all marketed HIV antivirals for a total of 330,000+ drug resistance tests in the study period. Approximately 1.5 million HIV antiviral retail scripts were dispensed and analyzed for the same period. 1) HIV resistance and antiviral prescribing was inversely correlated for NNRTIs i.e. resistance was highest for NNRTIs and its share of prescriptions was the lowest. 2) Although NRTI resistance was higher than PI resistance, NRTI prescribing was still significantly higher than PI prescribing across all regions. 3) HIV phenotypic resistance was statistically different by region for each class of drugs with the exception that there was no difference in resistance in the South compared to the West for NNRTIs. 2) There were also a number of statistically significant differences in antiviral prescribing by region for each class.

Conclusion: Phenotypic antiviral resistance for NNRTIs appears to be a major factor correlated with NNRTI prescribing. However, NRTI prescribing and NRTI resistance are both higher than PI resistance and PI prescribing, and not well correlated. Prescribing decisions may be influenced by other factors beyond resistance, including compliance, adverse events, and other considerations which will require further study.

OP 1.6.
Analysis of HIV-2 resistance to protease inhibitors

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Most studies of drug-resistance mutations have been focused mainly on HIV-1. Studies on HIV-2 have been much more limited due to the low number of HIV-2 infected individuals compared to HIV-1. Moreover, HIV-2 is predominantly found in West Africa, where treatment is often not available. Overall there is little overlap sequence identity between HIV-1 and HIV-2 viral genomes. Proteases display approximately 50% identity, and their structure is highly similar. Furthermore, the susceptibility of HIV-2 to protease inhibitors (PI) is largely unknown. We have investigated in this report the possibility that the presence of genotypic changes in the protease of HIV-2 protease can be associated with resistance to PI. We studied 32 individuals infected with HIV-2 undergoing therapy with PI in order to characterize the polymorphism of protease gene in the presence of drug. The highest aminoacid variability in HIV-2 protease was predominantly observed between positions 10 and 40 and between positions 70 and 90 aminoacid. Using a resistance assay, natural susceptibility of HIV-2 primary isolates to protease inhibitors was found to be 3-4 times higher than HIV-1. In vitro selection pressure with PI showed the appearance of similar mutations to HIV-1 together with new alterations.

Protease mutations in HIV-2 were compared with similar PI-resistance mutations in HIV-1, to evaluate similarity of resistance mechanisms in these viruses. For direct mutagenesis the protease gene of HIV-2_{rco} was used. The recombinant viral assay (RVA) was constructed by deletion of the protease gene and introduction of stop codon in the env gene of HIV-2_{rco} clone. Intracellular recombination was achieved between the linearized HIV-2 vector and amplified protease coding regions. Resultant viruses were used to infect P4 cells expressing β-galactosidase in presence of increasing concentrations of protease-inhibitor drugs. Results show that HIV-2 can develop alterations in the protease gene that confer resistance PI. These alterations occur in similar and different positions compared to HIV-1.

OP 1.7.
Polymorphism and Drug-selected Mutations in the Protease Gene of HIV-1 in Naive and Multi-treated Patient Isolates from the Seine-Saint-Denis District in France: differences between B and non-B subtypes

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Phenotypic analyses of HIV-1 isolates have allowed to define anti-protease treatment algorithms which can be deduced from the amino-acid sequence of the protease gene. However, most of the collected data were obtained from HIV-1 subtype B isolates, and only few information are available concerning HIV-1 protease gene mutations in non-B subtypes. We have collected and analyzed the protease sequences of 49 naive patients (24 subtype B and 25 subtype non-B), and 530 multi-treated patients (405 [76,4%] subtype B and 125 [23,6%] subtype non-B). On the one hand, the sequences were interpreted according to Stanford "virtual phenotype algorithm". On the other hand, sequences were aligned and statistically analyzed in order to detect eventual subtype-related differences in protease sequence profiles.
In the naive group of patients, 3/49 isolates displayed anti-protease resistant mutations, either to both saquinavir and nelfinavir, or to nelfinavir only. Moreover, amino-acid substitution was significantly different between B and non-B subtypes in 8 positions of the protein, including positions 20 and 36, which are considered to be associated to drug-resistance. Finally, in 1 isolate (subtype non-B), an Asparagine was inserted at position 38 of the protease.In the multi-treated group of patients, the Stanford virtual phenotype algorithm indicated a significantly higher prevalence of anti-protease resistance in subtype B isolates than in the non-B (48% versus 36%; p=0.016). Analysis of the amino acid substitutions in the sequences of the protease showed that 22 positions are significantly different between B and non-B isolates. These positions included 7 sites associated to drug-resistance (10, 20, 30, 36, 50, 63, and 90), even though no significant difference of treatment exposure between B and non-B isolates was encountered. Our results indicate that the protease amino-acid substitution profile is different in B and non-B isolates and suggest that the algorithms of interpretation of the sequences to treatment strategies should be adapted to the virus subtype. They also suggest that treatment algorithms based on subtype B cohort studies might need modifications to be applied effectively on non-B subtypes isolates. Efforts should be considered to study each subtype independently.

OP 2.1.
Initial Treatment Strategies

Dr. Marianne Harris and Dr. Julio Montaner
Vancouver, Canada

Recommendations concerning the timing of antiretroviral therapy initiation have undergone significant changes in recent years. These changes have been driven by growing concern over long-term toxicities of antiretroviral drugs and the consequences of chronic exposure to these agents, including their impact on cardiovascular morbidity and mortality. The strategy of deferring initial antiretroviral therapy is supported by population-based data demonstrating consistently low rates of HIV disease progression when patients commence antiretroviral therapy at CD4 cell counts of 200/mm3 or higher. Hence some international guideline panels now advise that, in asymptomatic HIV-infected patients, antiretroviral therapy can be delayed until the CD4 cell count approaches 200/mm3, without compromising the effectiveness of the treatment. In addition, there is increasing evidence to suggest that AIDS-free patients who started therapy at higher CD4 cell counts, and are currently experiencing virologic suppression and immunologic reconstitution on antiretroviral therapy, can safely interrupt therapy for many months under close monitoring. Consideration is given to restarting antiretrovirals according to the same CD4 thresholds as for initial therapy. The potential benefits of this strategy - in terms of reducing drug toxicities and costs by reducing overall exposure to antiretroviral drugs - are readily apparent; however, the long-term immunologic and clinical impact of this strategy remains to be established.
Once the need for antiretroviral therapy has been determined, a number of options exist for drug combinations that have demonstrated acceptable safety and efficacy in clinical trials. Recent data indicate that triple nucleoside regimens are a suboptimal choice for initial therapy, except in certain specific circumstances. Currently recommended treatment regimens comprise two nucleoside or nucleotide analogues plus either a nonnucleoside reverse transcriptase inhibitor (efavirenz or nevirapine) or a ritonavir-boosted protease inhibitor. For the latter, the most supporting data are presently available for lopinavir, but suitable alternatives include saquinavir, indinavir, and possibly amprenavir or atazanavir.

OP 2.2.
New Anti-retroviral Strategies

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Current HAART uses combinations of NRTIs/NNRTIs, or NRTIs/PI, or 3 NRTIs, taken daily. Once started, treatment is continued indefinitely. New strategies, currently being explored in clinical trials, include:

1) Scheduled Treatment Interruptions (STIs), for three reasons: (1) stimulation of the anti-HIV immune response, (2) reduced toxicity, and (3) reduced costs. In carefully selected patients treated mostly with PI/NRTI combinations, selection of resistant pseudospecies has not been a problem. However, hopes for immune stimulation have been dashed. Large comparative trials are ongoing to test whether there are toxicity and cost advantages to STIs.

2) Treatment with PIs only. Ritonavir-boosted PIs reach plasma levels which exceed inhibitory concentrations by several orders of magnitude. Multiple mutations are necessary before HIV becomes resistant to these high drug concentrations. PI-only therapy is being explored for drug-naïve patients (with lopinavir/r), for maintenance therapy after successful conventional HAART (indinavir/r and azatanvavir/r), and for salvage therapy (lopinavir/saquinavir, and lopinavir/saquinavir/azatanavir).

3) The CCR-5 antagonists which are entering phase 2 and phase 3 trials have peculiar pharmacokinetics in that they block the receptors (or promote their disappearance from the cell surface) for a long time after administration, irrespective of plasma levels. It is therefore possible that these drugs can be administered at longer intervals, perhaps twice or once weekly.

OP 2.3.
Managing Therapeutic Failure

No abstract available

OP 2.4.
HIV Resistance & Therapeutic Strategies / Résistance du VIH et Stratégies Thérapeutiques

Carlo Federico Perno, Valentina Svicher, Mariella Santoro, Caterina Gori, Roberta D'Arrigo, Maria Concetta Bellocchi, Sara Giannella, Ada Bertoli, Federica Forbici, Andrea Antinori, Francesca Ceccherini Silberstein
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During its spread among humans, HIV-1 has developed an extraordinary degree of genetic diversity. Several factors are known to contribute to the generation of new viral variants and to influence the speed with which these viruses evolve: a) the error-prone nature of the RT, which lacks proofreading functions; b) the recombination between the two strands of the dimeric RNA genome, carried out by the RT enzyme during proviral DNA synthesis; c) the high rate of virus production that sustains HIV-1 infection in vivo; d) the rapid selection for viruses with different fitness, mainly due to immune pressure, co-receptor selection and antiviral therapy.
The pol region, encoding for viral enzymes such as RT and protease (PR), is subjected not only to natural variation, but also to the selection pressure imposed by the pharmacological treatment. Under these conditions, the virus is able to escape from antiviral drugs by accumulating new mutations, either alone or in clusters. The patterns of mutations accumulated by HIV under drug pressure are quite variable, depending from the level of pharmacological pressure, the backbone of virus strains, the length of therapy, etc. This makes quite difficult the definition of clear and consistent patterns of mutations associated to resistance to antiviral drugs. Indeed, with few exceptions, quantitative resistance to antivirals cannot be accurately predicted by current standard algorithms used in clinical practice.
Is the ability of HIV to mutate unlimited, depending from the type and amount of pressure given by antivirals, or are there areas of HIV-enzymes that cannot mutate without losing their functionality? This point, still unclear, has an enormous relevance in clinical practice, since it can help in designing new therapeutic strategies aimed to press the virus to mutate at key aminoacids crucial for the maintenance of sufficient viral fitness. The resulting virus may be replicating at a pace so limited that its ability to damage the immune system, as well as to further mutate to compensate such loss, is minimal.
For these reasons, we undertook a deep investigation aimed to define the conserved areas of RT and PR under pressure of antivirals. The results, presented in details in the lecture, show the presence of RT- and PR-regions highly conserved even under deep therapeutic pressure. Interestingly, such areas represent 50% and more of the total aminoacid sequences, and are distributed in long and short stretches located in various areas of both enzymes. Site-directed mutagenesis studies show that the variation of single aminoacids in these conserved areas causes a deep loss of HIV fitness, down to total inability to replicate. Further analyses show that other mutations, beyond those known to be asssociated with resistance to antivirals, seem to be associated with resistance to some antivirals. A confirmation of their relevance in clinical practice may help in defining more precise algorithms able to correctly predict the efficacy/resistance of antivirals.

OP 2.5.
Effects of Baseline Protease Inhibitor (PI) Mutations on the Efficacy of Ritonavir-Boosted Atazanavir (ATV/RTV) and Lopinavir/Ritonavir (LPV/RTV) in Patients Who Have Experienced Virologic Failure on Multiple HAART Regimens

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Background: ATV is a potent once-daily PI with durable efficacy in naïve patients and in experienced patients (when boosted with RTV). BMS AI424-045 compared the efficacy and safety of ATV boosted with RTV, or in a dual-PI regimen with saquinavir, to that of LPV/RTV as part of combination antiretroviral therapy in HIV-infected patients who had been administered at least 1 PI, NNRTI, and NRTI in 2 or more failed HAART regimens.

Methods: A post-hoc analysis was performed using the "Stanford Panel" of 16 ATV- or LPV-associated mutations (10, 20, 24, 32, 33, 36, 46, 48, 50, 54, 63, 71, 73, 82, 84, 90) to determine if the number of baseline PI mutations (<4 or ≥4) influenced antiretroviral efficacy in patients receiving ATV/RTV 300/100 mg qd or LPV/RTV 400/100 mg bid, each combined with tenofovir 300 mg qd and 1 NRTI.

Results: 48-week results are shown.

	ATV/RTV			LPV/RTV		
	Overall mutations N=120	<4 PI mutations n=80	≥4 PI n=40	Overall mutations N=123	<4 PI mutations n=76	≥4 PI n=47
HIV RNA (mean change from baseline, log10 c/mL)	-1.93	-2.13	-1.38	-1.87	-2.10	-1.47
Responders (% of patients)*	53	68	25	54	66	36

*Patients with confirmed HIV RNA<400 c/mL without intervening replicated rebounds, study discontinuations, or CDC Class C AIDS events

Virologic failure, defined as no confirmed response (HIV RNA<400 c/mL) through 48 weeks while remaining on study or a confirmed virologic rebound (HIV RNA>400 c/mL) after a confirmed response, occurred in 32 of 120 (27%) and 36 of 123 (29%) of the ATV/RTV- and the LPV/RTV-treated patients, respectively, through 48 weeks.

Conclusions: ATV 300 mg boosted with RTV 100 mg qd demonstrated efficacy similar to that of a standard of care (LPV/RTV) in treatment-experienced patients at 48 weeks regardless of the number of baseline PI mutations. The magnitude of response to treatment with either ATV/RTV or LPV/RTV was inversely related to the number of baseline PI mutations (<4 or ≥4). A comparable diminution in response was observed in both study arms in patients with ≥4 baseline PI mutations. Because of small subgroup numbers, these data should serve only as a guide to therapy decisions.

OP 3.1.
HAART-induced Immune Reconstitution: limitations & prospects

No abstract available

OP 3.2.
New Insights into Immune Reconstitution. The pleiotropic effects of IL-15

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IL-15 exhibits many activities in common with IL-2, including induction of NK cell activity and cytolytic effector cells. The overlapping biological activities of IL-15 and IL-2 are attributable to the utilization by these cytokines of two common receptor chains ß and γ. NK cells are a critical component of host immune response to a variety of pathogens and they were originally identified on a functional basis because of their ability to kill certain tumor cells without previous stimulation. However, unlike T cells, they do not express clonally distributed receptors for antigen, and their function is finely regulated by a series of inhibitory or activating receptors.

The inhibitory receptors, specific for MHC class I molecules, allow NK cells to discriminate between normal cells and tumor cells (that have lost the expression of MHC class I) or virus-infected cells. Inhibitory NK cell receptors (iNKRs) also regulate the function of CD8 T cells. Whether increased expression of iNKRs on NK cells and $CD8^+$ T cells contributes to defective antiviral activity in HIV-infected individuals is not yet clear. We have analysed the expression of iNKRs (CD94, p158a, p158b and NKB1) on various cell subsets from asymptomatic untreated HIV-infected patients, patients under HAART and healthy donors. We found that HIV-infection leads to abnormal cell-surface expression of these receptors on NK cells, CD4, CD8 T cells, and γδ T cells, and the up-regulation of iNKRs is a consequence of HIV viremia. The influence of iNKRs expression on effector functions was analysed by the detection of intracellular TNFα and IFNγ production in $iNKRs^+$ and iNKRs subpopulations following ex-vivo stimulation with SEB for T cells or K562 for NK cells. It appeared that responding cells are mostly found in the iNKRs- subset, and exogenous addition of IL-15 decreases the expression of iNKRs in the expressing subsets and concomitantly enhances the production of TNF- α ereforeIL-15 can restore the effector functions of T cells and NK cells by modulating the expression of NKR.

Another feature of IL-15 is its ability to act as a survival factor. CD4 and CD8 T cells from HIV-infected individuals are highly susceptible to spontaneous, CD95/Fas and TNF-R-induced apoptosis, and this sensitivity may impair their ability to control HIV-infection. We reported that IL-15 exhibits a strong survival effect on total CD4 and CD8 T cells from HIV-infected individuals, and the anti-apoptotic effect of IL-15 was linked to its ability to up-regulate Bcl-2. In addition, HIV-specific CD8 T cells were found to down-regulate Bcl-2 expression, which was restored by IL-15, concomitantly with an increased survival of these cells.

In conclusion, IL-15 could affect the immune response of HIV-infected patients at different levels, first by stimulating innate immunity through the modulation of iNKRS and enhancement of effector functions, and second by restoring adaptive immunity through the maintenance of HIV-specific effectors by increasing their survival. These observations could provide new implications for immune-based therapies in HIV-infection.

OP 3.3.
State of the Art of anti-HIV Immunotherapy

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The advent of HAART has radically changed the clinical course of HIV infection. However, recent advances in the pathogenesis of the infection, including the analysis of T cell dynamic changes induced by the virus and HIV-1 cellular reservoirs, emphasize the fact that HIV-1 eradication will not probably occur even following a life-long use of effective antiretroviral therapy.
The vanished goal of eradicating HIV infection by combining several antiretroviral agents has refocused most of the attention on strategies aimed at the long-term management of HIV disease. Among these, immune-based interventions which include antiretroviral drugs in combination with compounds that are able to modulate the function and reactivity of the immune system might be pursued. The goal of these strategies is to achieve the long-term control of virus replication with a minimal or possibly no use of antiretroviral drugs. In this context, it is worth exploring the potential use of immune modulating drugs, such as mycophenolic acid, that thank to their mechanism of action may also exert an antiviral activity.
In this context, the possibility of combining antiviral and immune-based approaches has a solid basis in the consolidated experience of IL-2 administration. Multiple trials on different cohorts of infected individuals have shown that intermittent administration of 3-12 MIU/d of IL-2 can restore normal levels of circulating CD4+ T-lymphocytes, a crucial parameter of immune function. Retrospective analysis of individuals who have received IL-2 in previous years is encouraging in the hypothesis that the observed increases of CD4+ T-cell counts are not a simple "cosmetic" change in the composition of PBMCs of these individuals. Hopefully, ongoing phase III clinical trials will address this fundamental question. An added value of IL-2 experimental therapy is its broader implication: administration of a cytokine, a messenger protein that allows the intercellular communication among immune cells, as a drug to immunodeficient individuals may lead to the reconstitution of their immune responses, thus increasing their capacity to fight opportunistic infections and tumors.

OP 3.4.
The Future of HIV Vaccine Development

Richard A. Koup, MD

While most vaccines have been developed by an empiric approach, the development of a vaccine against HIV will likely be based upon an understanding of the role of the immune system in protecting against HIV replication in infected individuals.
Development of a vaccine that stimulates neutralizing antibodies to HIV has been extremely challenging. The envelope of HIV has many ways of avoiding the affects of neutralizing antibodies, but newer approaches may get around these viral defenses. In contrast, we have made major strides in developing vaccines that stimulate CD4+ and CD8+ T cell responses against HIV. Whether these T cell vaccines will be effective in the absence of neutralizing antibodies remains to be seen.

There is reason to be optimistic that a vaccine against HIV will be able to be developed. HIV transmission is relatively inefficient, and certain aspects of the virus must be conserved in order to allow entry. In addition, there are examples of natural protection against HIV infection or disease progression. Finally, animals have been able to be protected from AIDS retrovirus infections after vaccination.

Historical methods of vaccine production include the use of attenuated viruses or whole killed virus. Because of the uniform lethality of infection with HIV, there are potential problems with both of these approaches. Newer methods of recombinant DNA technology are therefore being used to develop vaccine products that should generate both humoral and cellular immune responses against HIV. Many of these are already in various phases of clinical testing. A rational and scientific approach will hopefully lead to the development of a protective vaccine against HIV.

An initial Phase I study (VRC 004) evaluating a 4-plasmid DNA combination of B clade gag/pol/nef with envelope from clades A, B, and C has been completed in 50 healthy adults in the U.S., with no vaccine-related serious adverse events. The study evaluated doses of 2, 4, and 8 mg delivered by a needless injection device. CD4+ and CD8+ T cell responses were detected in the majority of vaccinees using peptide pools to stimulate PBMCs followed by IFN-g ELISpot and flow cytometric detection of intracellular IL-2 or IFN-g production. HIV-specific antibody response was detected in 12/40 subjects. Responses could be detected after two injections, and the responses to the 4 and 8 mg doses were greater than those to the 2 mg dose. The full immunology and development program for this vaccine will be presented.

OP 3.5.
Humoral Immune Response Monitoring in HIV-1-infected Patients under anti-Tat Therapeutic Vaccine Trials

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The early synthesized Tat protein in its extracellular configuration exhibits pathogenic effects on both paracrine infected cells (enhancement of viral replication) (Re MC, La Placa M et al. 1995) and uninfected immunocytes (immunosuppression) (Zagury D et al., 1996 ; Cohen S, Pardee M et al., 1998; Gallo RC, 1999). To neutralize extracellular Tat and counteract its toxic effects anti-Tat therapeutic vaccines have been developed and are currently under clinical trials (Gringeri et al., 1998; Cafaro A, Ensoli B et al., 2002; Aventis Pasteur, 2002). Neutralizing anti-Tat Abs representing a major parameter to monitoring immunogenicity of the vaccine, we propose 2 functional anti-Tat Ab tests: the standard CAT assay to measure Tat-induced enhancement of viral replication and TRAIL mRNA synthesis by uninfected monocytes. Given that native Tat is unstable and some of its effects rapidly inactivated in serum, we present here standardized experimental conditions of the 2 Tat assays allowing for sensitive, quantitative and reproducible results.

OP 4.1.
Optimal use of Therapeutic Drug Monitoring in HIV Infection

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Therapeutic Drug Monitoring (TDM) is becoming more and more part of routine clinical practice, at least in Europe. Several studies have been published during the last years showing the benefit of using TDM to improve the management of HIV infected patients.
One of the drawbacks for using TDM in the recent past was the lack of consensus on the therapeutic range for antiretroviral drugs. Without the availability of a therapeutic range, TDM is nothing more than targeting at normal levels, without knowing whether these levels are subtherapeutic, therapeutic, or even toxic. In March of 2003, however, a consensus document was released by a group of expert HIV pharmacologists and is now available on www.HIVpharmacology.com.
Several guidelines are now more in favour of including TDM in the diagnostic make-up of new HIV infected patients. For using TDM in antiretroviral experienced patients, it is probably not enough to focus on drug levels, while no information on resistance patterns is available. The integration of pharmacological and virological parameters (the IQ concept) has been a theoretical concept for a long time, but data are now accumulating that this information can also be used in clinical practice. Finally, while the focus of TDM in the past has been on prevention of virological failure, more data are now accumulating demonstrating relationships also with toxicity. For instance, nephrotoxicity caused by indinavir, and CNS toxicitiy caused by efavirenz are 2 examples how TDM can be used to manage these toxicities. Limited data have become available that suggest that the same is true for hepatotoxicity due to nevirapine use, or lipid abnormalities after lopinavir use.

OP 4.2.
The Search For New Antiretroviral Drugs

Erik De Clercq, Leuven - Belgium

In recent years, significant progress has been made towards the chemotherapy (and - prophylaxis) of HIV infections. This prores is situated at three different levels. (i) New anti-HIV drugs have been approved for clinical use and have entered the market: the virus entry inhibitor enfuvirtide (Fuzeon™), the nucleoside reverse transcriptase inhibitor (NRTI) emtricitabine (Emtriva™), the nucleotide reverse transcriptase inhibitor (NtRTI) tenofovir disoproxil fumarate (Viread™) and the HIV protease inhibitor (PI) atazanavir (Reyataz™). (ii) Other compounds have proceeded through preclinical and/or clinical development: CXCR4 antagonists (e.g. AMD070), CCR5 antagonists (e.g. SCH-C, TAK-220, and spirodiketopiperazines), NRTIs (such as amdoxovir and other 2',3' dideoxynucleoside analogues), NNRTIs (such as capravirine, dapivirine and etravirine), integrase inhibitors (such as S-1360 and other diketo acid derivatives) and PIs (such as tipranavir). (iii) Yet other compounds, acting by novel mechanisms, have recently been identified as anti-HIV agents that seem worthy of further (pre)clinical development: cell receptor CD4 downmodulators (i.e. cyclotriazadisulfonamides), viral envelope gp120 binding agents such as plant lectins and glycopeptide antibiotics (aglycons), HIV integrase inhibitors such as the pyranodipyrimidine V-165, and two new classes of compounds (i.e. N-aminoimidazoles and pyridine oxide derivatives) which seem to interfere with a post-integration, transcription transactivation event. As a whole, the approaches for the treatment of HIV infections have in recent years become both more diverse and more efficient.

OP 4.3.
New Antiretrovirals and Strategies in the Gilead Pipeline

James F. Rooney, Andrew Cheng, William A. Lee - Gilead Sciences, 333 Lakeside Drive, Foster City, CA 94404

The development of new products for the treatment and prevention of HIV infection continues to be the primary focus of research and development activities at Gilead. In an effort to reduce pill burden and increase convenience, tenofovir DF (TDF) and emtricitabine (FTC) have been combined into a single tablet, which can be taken once daily. Recent pharmacokinetic data have shown that the fixed-dose combination (FDC) of TDF / FTC is bioequivalent to the individual dosage forms. An MAA and NDA for the FDC have been filed. New compounds in development include an amidate prodrug of tenofovir, GS-7340, and a new HIV-1 protease inhibitor, GS-9005. GS-7340 is selectively metabolized inside cells, which results in accumulation of tenofovir in certain cell types, such as lymphocytes. GS-7340 is 1000 fold more active than tenofovir against HIV in cell cultures. Following 1 hour incubation of GS-7340 with whole blood, the levels of tenofovir inside PBMCs were over 20 times greater than those after incubation of whole blood with tenofovir. A Phase 1 clinical study of GS-7340 has confirmed the potent anti-HIV activity of this compound and a phase 2 study in patients with nucleoside-resistant virus is planned. Using a similar technology for targeting of lymphocytes, Gilead has developed a new HIV-1 protease inhibitor, which accumulates in lymphocytes and is highly active against viruses which contain mutations associated with protease inhibitor resistance. A phase 1 dose ranging study is underway to determine the safety, tolerability, and pharmacokinetics of this compound. New strategies for the use of current antiretrovirals include several studies exploring the potential for tenofovir DF in pre-exposure prophylaxis in patients at high risk for acquiring HIV infection.

OP 4.4.

TMC114/Tibotec/ISHEID, June 4 2004
Eric Lefebvre, Yardley - USA

TMC114 is a next generation PI with potent in vitro antiviral activity against wild-type and PI-resistant HIV-1. TMC114-C207 was an open, randomized Phase IIa study in 50 multiple PI-experienced patients.The objectives of the trial were to assess the pharmacokinetics, antiretroviral activity, safety, and tolerability of the substitution of TMC114 in a non-suppressive antiretroviral regimen.
TMC114 was co-administered with a subtherapeutic dose of ritonavir (rtv) for 14 days in multiple PI-experienced, HIV-1-infected subjects.It was substituted for the PI(s) in the non-suppressive regimen; all other ARVs were unchanged. Patients received TMC114/rtv at doses of 300/100 mg bid, 600/100 mg bid, 900/100 mg qd or continued the non-suppressive regimen. After 14 days, TMC114 was discontinued and changes in ARVs were permitted.
Median baseline plasma HIV-1 RNA for the study group was 4.3 log10 and median baseline CD4 cell count was 305 cells/mm3. The median number of primary PI mutations was 3, while the median number of PI resistance-associated mutations was 6 (both primary and secondary mutations).Median change at day 14 in HIV-1 RNA was -1.38 log10 for all TMC114/rtv groups and +0.02 log10 for the control group. A reduction of 0.5 (or 1.0) log10 in HIV-1 RNA was achieved at any time point during treatment by 97% (76%) and 25% (17%) of subjects in all TMC114/rtv and control groups, respectively.
Treatment with TMC114/rtv was generally well tolerated. Most AEs were judged to be mild to moderate in severity and no dose relationship was observed. The most commonly reported AEs were GI events (diarrhea, flatulence) and central nervous system disorders (headache, dizziness). Two subjects in the TMC114/rtv groups prematurely discontinued treatment; one due to a combination of grade 2/3 GI and a grade 3 CNS (headache) event and the other due to esophageal candidiasis and stenosis (judged as HIV-related and unrelated to TMC114/rtv). One grade 4 hepatotoxicity in a patient in the 600/100 mg bid dose group was reported as a serious AE and was judged to be probably related to TMC114/rtv. This event resolved without sequelae upon discontinuation of all antiretrovirals.
Overall, TMC114/rtv exhibited potent antiretroviral activity and favorable pharmacokinetics when given for 14 days to multiple PI-experienced patients currently receiving a non-suppressive PI-containing regimen.

OP 4.5.

The Discovery and Exploratory Development of UK-427,857: A Novel CCR5 Antagonist for the Treatment of HIV

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The successful future management of patients infected with HIV requires the discovery and development of new agents that combine novel mechanism-of-action with pharmacokinetic, safety and toleration profiles that are consistent with chronic, durable therapy. It is against this backdrop, that the inhibition of HIV fusion and entry into immune function cells is one of the most promising approaches to discovering new classes of anti-retroviral agents that have the potential to meet the aforementioned target profile.

UK-427,857 is a novel CCR5 antagonist and is the most advanced clinical candidate in Pfizer's CCR5 discovery and development programme. UK-427,857 is exquisitely selective for the CCR5 receptor and inhibits viral replication by blocking the binding of viral gp-120 to the CCR5 receptor.This translates to potent activity in vitro against both lab-adapted and primary clinical HIV isolates spanning all of the clades, including viruses that are resistant to current classes of HIV agents.

UK-427,857 has been evaluated in >400 volunteers and HIV patients where it is well tolerated at doses in excess of those required to block the CCR5 receptor and those providing free drug levels above the in vitro concentrations for potent antiviral activity. Consistent with this, UK-427,857 has demonstrated encouraging short-term (10 day), single agent efficacy as measured by reductions in viral loads in asymptomatic HIV patients; CCR5-tropic patients receiving 100mg BID showed a mean decrease in viral load of 1.42log10 from baseline to day 11, whereas a dose of 25mg QD produced a mean viral load reduction of 0.42log10.

The clinical pharmacology of UK-427,857 has been studied extensively in volunteers. It is a substrate for cytochrome P-450 3A4 (CYP 3A4) and the p-glycoprotein transporter, but it does not significantly inhibit or induce CYP P-450 3A4 or other cytochrome P-450 enzymes. Studies both with CYP 3A4 inhibitors and inducers have demonstrated that UK-427,857 will have manageable drug interactions when used in the setting of HIV patients receiving current HAART.

In summary, UK-427,857 is a novel CCR5 antagonist with potency, pharmacokinetic and toleration profiles that merit its further evaluation as a new therapy for patients with HIV/AIDS.

OP 4.6.
BMS-488043: A novel, small-molecule HIV-1 attachment inhibitor

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The recently discovered HIV-1 Attachment Inhibitors (AIs) induce conformational changes within the viral envelope gp120 protein and inhibit attachment to cellular CD4 receptors. Potent and selective inhibition is observed in vitro against macrophage-, T-, and dual-tropic HIV-1 strains. Consistent with our previous results, a series of biochemical studies show that AIs such as BMS-488043 and BMS-378806, prevent sCD4 binding to gp120. AIs bound readily to gp120, but could not bind to or displace sCD4 from pre-formed gp120/sCD4 complexes. Compound inhibition was greatly reduced with increasing concentrations of sCD4 in a gp120/CD4 binding ELISA assay. Collectively, these results indicate that AIs function by blocking gp120/CD4 interaction and that binding of AIs and sCD4 to gp120 is mutually exclusive. Mapping studies show that deletions of V1, V2 and V3 loops had a significant impact on AI binding. Circular dichroism spectrum shifts, changes in the rate of thrombin cleavage of the V3 loop when AIs are bound, and significant decreases in the binding of CD4i and CD4BS MAbs to gp120 upon AI binding confirmed that AIs induce gp120 conformational changes when bound. Phenotypic and genotypic analysis of drug selected virus variants showed that selected resistance substitutions span the viral envelope, with at least 9 residues identified at CD4 specific contact sites. These data are consistent with compounds sharing interaction sites with CD4 and binding to a pre-CD4 form of gp120.

The antiviral activity, safety, and tolerability of AI BMS-488043 were evaluated in a placebo-controlled ascending multiple-dose study in HIV-1-infected adults. Oral administration of 800 or 1600 mg doses vs. placebo q12 hr for 8 days were evaluated over a 14 day period with daily viral load (VL) monitoring. In subjects receiving the 1600-mg dose of AI BMS-488043, 67% (8/12) had a VL decline >1.0 log10, with 42% (5/12) having a VL decline >1.5 log10. None of the placebo treated subjects exhibited a VL drop of 0.4 log10. BMS-488043 was well tolerated and there were no serious adverse events and no discontinuations from the study. This proof-of-concept study validates the AIs as a novel class of antiretrovirals with potent antiviral activity in HIV-1-infected subjects. Further development of AIs are clearly warranted.

OP 4.7.
Identification and characterization of the determinants of activity of the HIV-1 maturation inhibitor PA-457

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We have previously demonstrated that the betulinic acid derivative, PA-457, potently inhibits HIV-1 replication by targeting a late step in Gag processing (Li, et al., Proc Natl Acad Sci U S A. 11:13555-13560, 2003). Specifically, PA-457 blocks the conversion of the capsid precursor (CA-SP1, p25) to mature capsid protein (CA, p24) resulting in the release of immature, non-infectious viral particles. Consistent with this novel mechanism of action, PA-457 retains activity against virus isolates resistant to the currently approved classes of HIV therapeutics. Results from in vitro selection experiments indicate that determinants of PA-457 activity reside in the region flanking the Gag CA-SP1 cleavage site. This presentation will describe our efforts to identify and characterize the molecular determinants of PA-457 activity.

OP 4.8.
Pharmacological Evaluation of SPD754, a New NRTI

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Background: SPD754 is a deoxycytidine analogue (dCA). The pharmacokinetics (PK) of both SPD754 in plasma and SPD754-triphosphate (SDP754-TP) in PBMCs have been shown to be linear across a range of doses up to 800mg bd in man. 10 days monotherapy with 1200mg/day (600mg bd or 1200mg qd) in treatment naive patients resulted in a 1.65 log10 mean reduction in HIV-1 RNA. M184V confers a median 1.8-fold change in susceptibility to SPD754. The addition of up to 5 TAMs also confers a median 1.8-fold change. SPD754 is therefore likely to be effective for the treatment of both ART naïve and experienced patients. SPD754 and 3TC have additive antiviral activity against wild-type HIV-1 in vitro but, in common with other dCAs, share a common intracellular anabolic pathway. The effects of SPD754 and 3TC on each other's intracellular phosphorylation were investigated in vitro, as was the influence of 3TC on the antiviral activity of SPD754. 3TC and SPD754 were administered to human volunteers alone or in combination to determine the PK profiles the parent compounds in plasma and of their intracellular TPs in PBMCs.

Methods: PBMCs were incubated in vitro in the presence of fixed concentrations of [^{3}H]SPD754 and unlabelled 3TC, or [^{3}H]3TC and unlabelled SPD754. Intracellular concentrations of labeled phosphorylated metabolites were determined by HPLC. The antiviral activity of SPD754 against a recombinant HIV-1 containing the M184V mutation was assessed in activated PBMCs at a range of 3TC concentrations. In the human volunteer study, 21 male HIV-ve subjects received either SPD754 600mg bd, 3TC 300mg qd or both in random order for 4 days (with ≥7 day washout). Extensive PBMC and plasma sampling was undertaken after the final dose in each period. Parent plasma and intracellular TP concentrations were assayed by HPLC.

Results: The entry of SPD754 and 3TC into PBMCs was unaffected by each other's presence. 3TC reduced intracellular SPD754-TP concentrations in a dose dependent manner, with 3μM 3TC reducing SPD754-TP by 4-6 fold relative to its concentration determined in the absence of 3TC. SPD754 had no effect on intracellular 3TC-TP concentrations. The IC_{95} value of SPD754 against M184V HIV-1 was increased 2-4 fold by the addition of 3TC. The human plasma PK of SPD754 and 3TC, and the intracellular PK of 3TC-TP, were un affected by co-administration. In contrast, intracellular SPD754-TP concentrations were reduced approximately six-fold in the presence of 3TC.

Conclusions: Evaluation of the intracellular TP concentrations of NRTIs in combination is essential as plasma PK studies may not predict intracellular effects. SPD754 has promising antiviral activity against viruses harboring M184V and multiple TAMs. However the marked reduction in intracellular SPD754-TP concentrations in the presence of 3TC, resulting in antagonism of their antiviral activity, indicates their co-administration, and potentially that of other dCAs, is likely to be unsuitable for clinical practice.

OP 5.1.
Management of metabolic complications of antiretroviral therapy

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The past several years have witnessed a dramatic reduction in HIV-associated morbidity and mortality in the developed world, an event that is generally attributed to the advent of highly active antiretroviral therapy (HAART). However, the enthusiasm generated by this therapeutic advance has been tempered by widespread reports of potentially deleterious metabolic side effects, including insulin resistance, dyslipidemia, and changes in body fat distribution that include syndromes of both fat accumulation (visceral adiposity, buffalo hump) and fat loss (lipoatrophy). Studies performed in large cohorts in countries with widespread access to HAART suggest that nearly 50% of individuals develop the morphololgic features of this syndrome. Given the similarity to metabolic syndrome X, which has been associated with increased risk of cardiovascular disease, it is feared that these side effects may impact on the long-term prognosis in patients whose life expectancies have been significantly extended due to effective viral suppression by HAART. This presentation will focus on current treatment options for the so-called lipodystrophy syndrome including: changes in the antiretroviral regimen (e.g. PI-sparing regimens, alterations in the nucleoside backbone); cardiovascular risk reduction with lipid-lowering agents (e.g. statins, fibrates) and life-style modification (e.g. diet and exercise); insulin-sensitizing agents (e.g. metformin, thiazolidinediones); and lipolytic agents (e.g. recombinant human growth hormone). The theoretical basis for and preliminary data supporting evaluation of experimental therapies (e.g. recombinant human leptin, recombinant human insulin-like growth factor I) will also be discussed.

OP 5.2.
Update on HAART-induced lipodystrophy

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The lipodystrophy syndrome frequently observed in HIV-infected patients often associates peripheral lipoatrophy, central hypertrophy and metabolic disorders but this set of alterations is not always present. In addition to factors related to the infection and to the patient, the treatment plays a major role in the occurrence of these alterations. Clinical data suggest that NRTI therapy is associated with peripheral lipoatrophy while treatment with PI increases the severity of lipodystrophy and of metabolic disorders.

To better approach the pathophysiology of the drug effects, in vitro adipocyte cell-models were used. An short-term inhibitory effect of PI on glucose transport was reported by the group of Mueckler. In long-term conditions, we observed that thymidine analogues, d4T and ZDV, contrary to other NRTI, can alter mitochondrial functions. Some PI but not all were able to strongly affect adipocyte differentiation possibly by targeting the step of the adipogenic differentiation factor SREBP-1. This could result from an altered structure of the nuclear lamina network due to impaired maturation of the lamina protein, lamin A. Thymidine analogues did not impair adipocyte differentiation but altered adipocyte lipid content. PI, contrary to NRTI, induced insulin resistance. Finally, some PI and thymidine analogues markedly altered adipocytokine expression and secretion : while IL-6 and TNFα were increased by the drugs, adiponectin was decreased. The altered secretion of IL-6 and TNFα was parallel to the extent of drug induced-apoptosis. Thus, in vitro, NRTI and PI could alter different adipocyte functions and could act in synergy to induce lipid loss and apoptosis ultimately leading to fat loss.

In vivo studies revealed that NRTI could play an important role in lipoatrophy not only by decreasing mitochondrial DNA but also by other mechanisms. Lipoatrophic adipose tissue from patients presented major histological alterations with decreased adipocyte size, increased fibrosis and macrophage infiltration. This tissue had an altered differentiation and insulin sensitivity. The profile of adipocytokines was markedly altered with increased TNFα and IL6 and decreased adiponectin and leptin expression. In addition, as in vitro, expression of TNFα and IL6 was parallel to the level of cell apotosis suggesting that these cytokines play an important role in fat loss. These data, together with in vitro data, suggest that ART-induced lipoatrophy could result from the synergistic effect of NRTI and PI which could alter adipogenic transcription factors, adipocytokine secretion, mitochondrial function resulting in decreased differentiation, adipose insulin resistance and apoptosis ultimately leading to lipoatrophy. Visceral fat hypertrophy could be explained by the different physiology of visceral adipocytes which could became hypertrophied due to increased local cortisol synthesis.

Metabolic alterations observed in ART-treated patients could result from the direct effect of drugs on lipid metabolism or insulin sensitivity. In addition, due to lipodystrophy, adipose tissue has an altered pattern of adipocytokine secretion with decreased adiponectin and an increased release of free fatty acids. This with aggravate metabolic disorders and insulin resistance.

OP 5.3.
In vitro Suppression of the Lipogenic Pathway by the non-nucleoside Reverse Transcriptase Inhibitor Efavirenz in 3T3 and Human Preadipocytes or Adipocytes

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A serious metabolic syndrome combining insulin-resistance, dyslipidemia, central adiposity, and peripheral lipoatrophy has ansen in HIV-infected patients receiving highly-active antiretroviral therapy. The aim of this work was to examine the effects of the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz on adipocyte differentiation and metabolism. When induced to differentiate in the presence of efavirenz (5-50 µM), 313-F442A preadipocytes failed to accumulate cytoplasmic triacylglycerol droplets. This phenomenon was l-apidly reversible, and was also readily detectable in the 313-L1 preadipose cell line, and in primary cultures of human preadipocytes. When applied to mature 3T3-F442A adipocytes, efavirenz induced a delayed and moderate reduction in cell triglyceride content. Measurement of [3H]-deoxyGlucose uptake, basal and agonist-stimulated lipolysis, and cell viability indicated that these pathways are not involved in efavirenz effects on triacylglycerol accumulation. By contrast, we found that the NNRTI induced a dramatic dose-and time-dependent decrease in gene and protein expression of the lipogenic transcription factor sterol regulatory element-binding protein-lc (SREBP-1c). Adipose conversion was only altered at the highest efavirenz concentrations, as suggested by the mild reduction in peroxisome proliferator-activated receptor-gamma and CCAAT/enhancer-binding protein-alpha. CCAAT/enhancer-binding protein-13 remained unchanged. The inhibition of SREBP-lc expression was accompanied by a sharp reduction in the expression of SREBP-lc target genes, and in the adipocyte lipogenic activity in efavirenz-treated cells. Finally, the inhibitory effect of efavirenz on cell triglyceride accumulation was prevented by directly providing free fatty acids to the cells, and was reversed by overexpression of a dominant positive form of SREBP-1c, reinforcing the implication of this transcnption factor in the anti-lipogenic effect of the drug. When considered together, these results demonstrate for the first time that the NNRTI efavirenz induces a strong inhibition of the SREBP-lc-dependent lipogenic pathway that might contribute to adipose tissue atrophy (J Biol Chem, in press).

OP 6.1.
HIV in Central & Eastern Europe

No abstract available

OP 6.2.
Family Systems Psychotherapy for Substance Abuse, HIV Care

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For last years chemical dependence, HIV acquired the epidemic range in Ukraine and in Vinnitsa oblast in particular. Statistics data certify from 189686 persons have formed the population of Vinnitsa oblast there are 23027 persons with alcohol abuse, 1134 with drug and 27 with toxic had been registered officially. So this quantity is larger to a great extent. Each 100-th citizen of Ukraine is HIV-infected. Medical establishments are engaged in physical symptoms of chemical dependence elimination, but mental, psychological sphere has been the core of dependence is almost out of physicians' field of vision. And different non-medicament psychological rehabilitation programmes, necessity and importance are obvious. Rehabilitation Center "Steps" over-all approach to the problem provides for psychotherapy of the family members without fail. Such approach is more effective as the practice displayed.

If the substance abuse and/or HIV is regarded as the whole family symptom, substance abuse, HIV care approach from family system direction point of view makes psychological problems of the substance abuse, HIV dysfunctional family more explicit and the psychotherapy of substance abuse and co-dependence becomes more effective.

Family is the open developed system has functioned due to interrelationship action pf two laws - the law of homeostasis maintenance and the law of homeostasis divergence. The family is open system (if it is healthy), and the members interact with each other and with surrounding systems (school, business, science, religion, state etc.). The family as the system has the following peculiarities:

- System as the whole is larger than the sum of its parts;
- Something has affected the system in the whole influences on each individual element inside the system;
- The affect or change in the state of one of the system part is reflected in the other parts of the system in the whole changing.

Main positions of the family approach in psychotherapy of substance abuse are the following.

- Family members are closely linked with each other and fix in their relations those alterations and aims have made for the problem behaviour appearance instead of each of the family member growth and development.
- The vital system is described with mutability (from entropy up to rigidity) with respect to large complex of stable, repeated pictures of interaction (stereotypes). Those pictures of interaction, behavior and aims can be interpreted as linear (while relations of cause and effect are fixed) or circulated (while the symptom and the problems in the family are in interrelationship, in the circulated sequence of events determination have influenced mutually on each member of the family).
- Family problems are often linked with adaptation dilemmas to some surroundings influence and alterations (horizontal stress factors). Those alterations can occur when one of the family members starts the abuse. Such fact can force the family to refuse from old stereotypes and to create new relations.

Healthy and "problematic" members of the family have the chance to display various types of reaction on feedback with the environment. And the feedback means the necessary for the adaptation changes system answer. Adaptation can be displayed in the alteration refusal. Dysfunctional family on the early stage of the substance abuse does not remark the abuse of one of the family members or excuses him, defends from reprimand or entourage negative attitude tî so, the person with substance abuse problem delegates responsibility of the abuse to the family members who take upon such state of affairs. Members of the harmonious family react quickly and coincidently to the internal and exterior situation. The feedback reaction is positive alterations in the family, the restoration and spontaneity and creativeness growth of the family members.

- From the system point of view alterations are not the one and only decision of the sole problem (stop the abuse and there will be no problems in the family), but the dilemma which needs the solution. The substance abuse family psychotherapy question of principle lies not in the symptom (substance abuse, HIV) deliverance, but what will happen in the case of its deliverance. The accent is transferred from the discussion of the problem who is the "symptom bearer", where is its reason and how to get out of on the problem how the family will function without it and what is the cost of its elimination.

Substance abuse family is dysfunctional; rigid family system has attempted to remain habitual stereotypes of interaction between the elements of own subsystems and another systems out of exterior conditions alterations dependence. So topical necessities îf the weakest family member, the substance abuse person are blockaded and the substance abuse problem makes progress. He becomes "the symptom bearer", has been able to afford old fully formed interrelations between the family members.

"Identified patient" is the member of the family, divergent behavior and psychological (substance abuse, HIV) problems of who are the direct ground of the family appeal to psychotherapeutic aid. "Identified patient" destroys rigid family rules. The psycho-therapeutic efficiency result is morphogenetic function - positive feedback, divergences to the side of family system variations intensification the goal of which is family system alterations and transition to the next stage. The main factor has led to positive an alteration in the family is despair. "If the family is in despair it changes if not it remains the former" (C. Vitacker).

OP 6.3.
HIV Infection in Estonia

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HIV infection associated with injecting drug use has been reported worldwide, and is established as the major cause of rapidly increased rates of HIV infection in several countries throughout Eastern Europe. In the newly independent states, large-scale HIV epidemics have been observed from 1995 onward, after introduction to injecting drug use (IDU) communities.

The number of HIV infected cases remained relatively low, despite the rapidly and substantially increasing sexually transmitted diseases (STD) rates (syphilis in particular) - the HIV epidemic began to develop only after it was introduced into the drug injecting community. Through 1999, only 96 cases of HIV had been reported nationally. The HIV epidemic has progressed since 1999 with: 390, 1474, 899 and 840 new HIV positive cases were reported in years 2000, 2001, 2002, 2003 respectively. According to the UNAIDS, an estimated 1% of the young adult population (aged 15-49) in Estonia are living with HIV infection - the highest estimates in Eastern Europe.

HIV infection is predominant in the IDU population; thus providing the most common route of HIV transmission to the general population -- a critical concern. As has been noted in other settings, IDU acquired HIV often serves as the conduit for the introduction of infection into the heterosexual non-drug using population. The dramatic increase of IDU acquired HIV infection with corresponding rates of STDs places the Baltics, high rates of sex risk behavior and inadequate knowledge regarding prevention of disease transmission places Estonia at high risk for an impending sexually and STD driven HIV epidemic.

OP 6.4.
Spread of the HIV/AIDS infection and STIs in the Slovak republic

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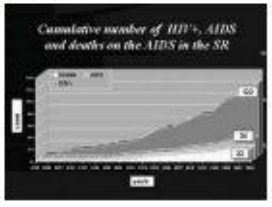
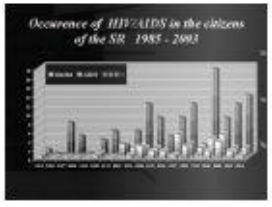
Slovak republic belongs to the countries with a very low incidence of the spread of HIV/AIDS infection and STIs. We would like to believe that this situation is a result of the good and corect administration of the preventive measurements. This prevention in our country has a very long tradition.

The surveillance of HIV/AIDS infection began in the Slovak Republic early in the 80-ies last century. The NRC for HIV/AIDS infection was established in the 1984. The first regulation about the HIV/AIDS prevention was published in the 1988. In this time in our country exists the National committee of the HIV/AIDS prevention and the National program of the HIV/AIDS infection in SR.. The activities in the HIV/AIDS and STI prevention are coordinate by our institution.

Since the beginnig till now were performed more than 3,5 million tests. In the last year were performed more the 150 000 examinations, but the count of these examinations has a decreasing trend.
The exact monitorng of this infection in SR began in the 1985. The cumulative number of registered HIV infections up to now is 122 cases. The clinical AIDS diseases developed in the 34 persons and 22 patients died.

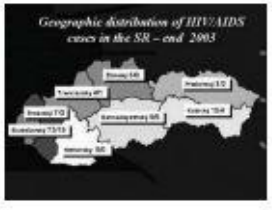


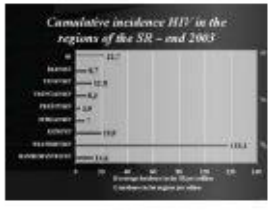


This graph shows the dynamic of the spread of the HIV infection, AIDS and deaths in the individual years. Increasing is variable and it is a favorable situation, that means that the dynamic of increase is not constant.

The spread of the HIV/AIDS infection in the individual regions of the Slovakia clearly shows that the occurence is the highest in the big agglomeration with the higher tourist traffic.

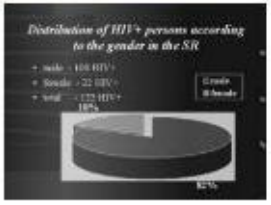
The highest concentration of the HIV infection and AIDS cases is in the capital Bratislava and its region. Second highest occurence is in the Košice region in the east of the Slovakia.

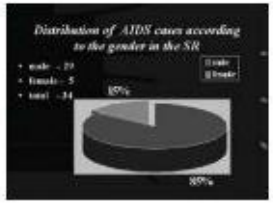




The average cumulative incidence per 1 million citizen in the SR is 22,7/1 000 000. The highest incidence is in the Bratislava region and this value is more than 5-times higher as the average. In the all rest regions the incidence is lower than the average value.

The majority of the HIV positive cases 82% are the men and the same situation is in the spread of AIDS disease 85%.



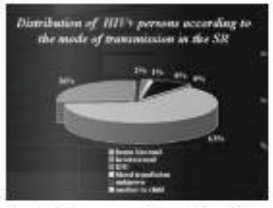


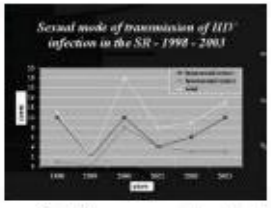
The next figure shows the distribution of the HIV positive cases according to the mode of transmission. The most frequent mode of transmission is the sexual contact. Nearly 89% from the all transmissions were caused through the sexual intercourses. From the sexual mode of transmission almost 72% creates transmission by the sexual intercourse in the group men who have sex with men.

The mode of transmission by blood transfusion was observed only in one case, by the blood transfussion abroad our country.

Relative favorable situation is in the group of the IDU-s. We have 2% of this mode of transmisioon only. In our country exist good preventive programms in this risks group.

It is necessary to show the fact that the mode of transmission from mother to child was not registered despite of the deliveries of the HIV positive women. In the age-group 0-14 years does occure no case of HIV positivity. The most of HIV positive cases exist in the age-group 20-34 years 62%.

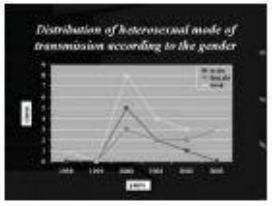


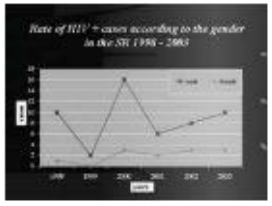


Analysis of the sexual mode of transmission shows that in our country dominates the transmission by the sexual intercours between the men who have sex with men and its ratio has an increasing tendency, and on the contrary the ratio of the transmission by heterosexual intercours goes down.
Analysis of the heterosexual mode of transmission shows that this mode of transmission is more frequent at the women than at the men.

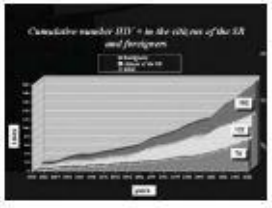
We can allege that in the period last 5 years the trend of the growth the number of the new infected people is not changed and the men dominate.

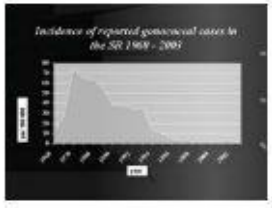
The big problem is a migration of the foreigners. The number of HIV positive persons who were detected in our country is 70.

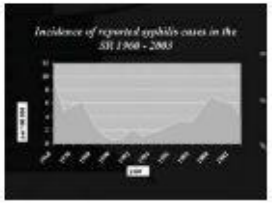




The situation about the STI is very similar to the situation in the neighbourly ountries. We can notice the growth of the syphilis and decrease in the gonococcal infections. But I have to remark that there is the situation in the reported cases.







OP 6.5.
The incidence of viral hepatitis markers among romanian teenagers with long-lasting horizontally acquired HIV inefction

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We studied the frequency of viral hepatitis markers in a sample of 161 Romanian teenagers' patients, mean age 13.9 years (standard deviation=1.2) with more than ten years long-lasting HIV infection, but without clinical or biochemical signs of liver disease. All the participants have horizontally acquired chronic HIV infection and 69% were under antiretroviral therapy. 126 patients (78.2%) were in CDC clinical stage B and only 35 in stage C. Overall, 126 (78.3%) children have markers of HBV infection (anti HBc positive) and 9 (5.6%) were anti HDV coinfected; only 3 (1.86%) have anti HCV antibody. A high prevalence of HBV replicative markers was found: 70 patients (43.5%; 95% CI=36.1-51.2) were HBsAg positive; 18 (11.2%; 95% CI=7-17) were HBeAg positive; while only 31 (19.2%; 95% CI=13.9-26.1) cleared the infection being antiHBs positive. To see the influence of advanced HIV infection on the evolution of HBV co infection we split the lot in two groups according with their immunological status. The prevalence of HBs antigenemia was 56.1% in severe immunodepressed children (CD4+ cells number <200) versus 36.5% in those with >200 CD4 cells (p=0.02), suggesting that the degree of immunosuppresion is correlated with the persistence of HBV replicative markers. The presence of HBV DNA was tested in all 32 HBsAg positive immunod pressed patients. Unexpectedly, 19 (59.4%) of these had undetectable levels of the replicative marker (<1000 copies/ml) and 13 have high viremic samples (>107 HBV DNA copies/ml). This finding supports the ideas that HBV is preferentially hepatotropic, but not directly cytopathic and that an efficient cellular immune response does not necessarily determine a favourable outcome even in the context of HBV/HIV co-infection.

OP 7.1.
Treatment of HIV-HBV Coinfection

Treatment of chronic HBV infection in HIV infected patients.
Yves Benhamou

Chronic infection with hepatitis B virus (HBV) affects about 5% of the world population. Among human immunodeficiency virus (HIV) infected individuals, the prevalence of chronic hepatitis B is 10 fold higher (10%) than in the general population. HIV/HBV co-infected patients have an increased risk of cirrhosis and liver-related death compared to HBV mono-infected patients. Due to the complex and potent interactions between HBV and HIV, as well as with the immune system and antiretroviral therapy, the strategy and management of anti-HBV therapy in HIV-infected persons must take into consideration both viral infections.
Lamivudine (LAM) is effective against both HIV and HBV replication. Among HIV/HBV co-infected patients, LAM (150 mg bid), given for HIV infection as part of an antiretroviral regimen, promptly inhibits HBV replication. However, HBV resistance to LAM (LAM-R) is observed in 50% and 90% of the cases after 2 and 4 years of therapy, respectively. The efficacy of adefovir dipivoxil (ADV) in HBV infected/HIV negative patients has been demonstrated against wild type, pre-core and LAM-R HBV. ADV has been shown to be effective and well tolerated in the treatment of LAM-HBV in HIV/HB co-infected patients. Four years of ADV in LAM-R HBV/HIV coinfected patients resulted in continuous decline of serum HBV DNA, with no mutation related resistance of both HBV DNA and HIV RNA reverse transcriptase. Tenofovir disoproxil fumarate (TDF) has recently been shown to have significant activity in HIV/HBV co-infected patients. TDF is approved for HIV infection and had shown to inhibit replication of wild type, pre-core and LAM-R HBV. Emtricitabine (FTC) has been also recently approved for the treatment of HIV infection. In recent studies FTC has demontrated activity against wild type and pre-core HBV in both HBV mono-infected and HIV/HBV co-infected patients. Nucleotides and nucleosides (NUCs) therapies are both effective for the control of HBV repication. LAM is associated with a high rate of HBV resistance. However, these treatments are associated with a low rate of HBe seroconversion. Combination therapy with NUCs may prevent HBV resistance. Although, no resistance to ADV was observed after 4 years of therapy when ADV was added to LAM. Combination therapies with pegylated interferon and NUCs may increased the seroconversion rate and are under investigation.
In summary, anti-HBV therapy should be considered in HIV coinfected patients who require anti-retroviral therapy. In patients with chronic hepatitis B who do not need anti-HIV therapy, AD therapy should be proposed.

OP 7.2.
Treatment of hepatitis C in HIV-coinfected patients

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Chronic hepatitis C affects one third of HIV-positive persons in Europe, but prevalence rises to >75% among IDUs. Progression to cirrhosis occurs faster and hepatocarcinoma may appear at younger age in this population. Chronic HCV infection increases the risk of liver toxicity using ARV drugs and may compromise immune recovery after beginning HAART. Guidelines for the management of chronic hepatitis C in the setting of HIV infection already have been published (International Panel. AIDS 2004;18:1-12).

The best candidates for anti-HCV therapy are HIV-positive subjects with proven chronic hepatitis C (positive HCV-RNA and elevated ALT), having CD4 counts >300 cells/mL and low plasma HIV-RNA (<10,000 copies/mL), with or without ARV therapy.

The combination of pegylated interferon (IFN) plus ribavirin (RBV) is the best choice of anti-HCV therapy, at doses used in HIV-negative individuals. However, early, end-of-treatment and sustained response rates are lower in HIV-positive patients than in HIV-negative counterparts. The results of two large trials (RIBAVIC and APRICOT) have been recently released and will be discussed in detail.

Quantitative monitoring of the virologic response to anti-HCV therapy seems to be useful in patient management. Patients that achieve a reduction in plasma HCV-RNA >2 logs at week 12 of treatment may benefit from continued therapy. For those who did not reduce HCV-RNA >2 logs at 12 weeks, the chance of cure is negligible, and thus treatment can be stopped. Patients with detectable HCV-RNA at 24 weeks of treatment may be also considered as failures, and discontinue therapy.

There is no evidence of any benefit from increasing the doses of either IFN and/or RBV in induction protocols. Extending treatment from 6 to 12 months in subjects with HCV genotypes 2 and 3 who had an early virologic response may increase their sustained response rate. Patients with HCV genotypes 1 and 4 with early virologic response should be treated for at least 12 months.

The risk of interactions between RBV and some NRTIs is of great concern. In particular, ddI should be avoided, due to the higher risk of hyperlactatemia and/or pancreatitis. AZT should also be used with caution due to the higher risk of anemia.

Finally, compliance with the medication should be strongly encouraged. In the face of mild side effects, managing these appropriately and/or reducing doses of either IFN or RBV would be preferable to stopping therapy.

OP 7.3.
Tolerance of Viral Hepatitis Therapy in HIV-infected Patients

No abstract available

OP 7.4.
Role of the hepatitis C virus-coinfection on humoral immune alterations in HIV-infected patients on HAART

Natalia Soriano-Sarabia, Sonia Molina-Pinelo, Carmen Delgado-Pecellin, Beatriz de Felipe, Armando Sanchez-Quijano, Eduardo Lissen, Manuel Leal, Alejandro Vallejo
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Objectives: Since the introduction of HAART the interest in humoral immunity alterations that induces chronic aberrant activation and immunodeficiency has rised. Our first aim was to analyze factors involved in both B cell count and B cell function disorders before the initiation of HAART in a closely followed cohort of 72 HIV-infected and naïve patients. Our second aim was to analyze long-term influence of HCV-coinfection (N=35) in reverting these alterations in the same cohort after 156 weeks on HAART.

Results: Before the initiation of HAART, HIV-infected patients showed B lymphopenia and polyclonal hypergammaglobulinemia compared to HIV-uninfected individuals (p<0.001). When this cohort of patients was analyzed according to HCV infection, no statistical differences in CD19, CD4 cell count and CD21low expression were found; instead IgG levels in HCV-coinfected patients were significantly greater than those found in HCV-uninfected patients (p=0.001). Moreover, beta-2-microglobulin level was higher among HCV-coinfected group compared to HIV-only infected patients (p=0.03). Besides, a strong negative correlation (p=0.005) between CD19 cell count and circulant IgG levels was found at baseline in the total of HIV-infected patients. This correlation was significant only among HCV-coinfected patients (p=0.005). During HAART, B lymphopenia and hypergammaglobulinemia slowly started to revert. At week 156 of treatment, normal values of CD19 cell counts were achieved, and although IgG levels were still increased compared to uninfected controls, they tended to normalize. Nevertheless, HCV-uninfected patients almost achieved normal CD19 cell counts and IgG levels after 156 weeks on HAART, while the HCV-coinfected group did not achieve normal values neither in B-cell counts nor in circulant IgG levels. Beta-2-microglobulin achieved normal values at week 12 after treatment among HCV-uninfected patients, while HCV-coinfected patients did it at week 48. After 60 weeks of treatment, levels of CD21low cells significantly decreased in the total HIV-infected patients (p=0.003), as well as among HCV-uninfected (p=0.037) and HCV-coinfected group (p=0.028).

Discussion: B cell lymphopenia at baseline may be explained by inhibition of naïve B cell proliferation by antigen:antibody complexes feedback regulation, massive differentiation into plasma cells, and also because immature precursors may be sequestered in bone marrow and lymph nodes. Basal correlation between CD19 cell counts and plasma IgG levels in the total HIV-infected patients was due to the presence of HCV. Thus, HCV activates B cells that proliferate and differentiate into antibody-secreting cells. Humoral immune system was chronically activated in HCV-coinfected patients and showed a delay in the recovery of normal humoral immune function because B cells have to differentiate into antibody-secreting cells in order to restrain HCV infection. Thus, immunoglobulin levels were still increased after three years on HAART. No differences in CD21 expression analysis were found between HIV-only infected patients and HCV-coinfected ones, suggesting that B cells were not activated by hepatitis C virus through CD21.

OP 7.5.
Liver Transplantation in Five HIV-infected Patients With Virus Hepatitis Induced Cirrhosis

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Introduction: Liver transplantation in HIV-infected patients with end-stage liver disease is under current debate. We report on our experiences with five HIV-infected patients, who underwent orthotopic cadaveric liver transplantation (OLT) at our transplantation center.

Methods: Between July 1998 and October 2001 five HIV-infected patients underwent OLT because of virus induced liver cirrhosis. One patient suffered from HBV-, three patients from HCV- and one patient from HCV/HBV/HDV-related cirrhosis. Mean duration of HIV infection was 15 years (range 12 - 17 years). Before OLT mean CD4 T-cell count was 299 cells/µl (range 86 - 621), mean viral load was 39926 copies/ml (range < 50 copies - 175000 copies/ml). Patients were prospectively followed-up with a mean duration of 25,6 months (range 3 - 61months).

Results: Three patients died three, ten and 31 months after OLT, respectively, due to graft failure. Causes of graft failure were: recurrent thrombosis of the hepatic artery, HCV-associated cholestatic hepatitis and chemotherapy-induced liver damage due to Hodgkin´s disease, which was diagnosed 17 months after OLT, in addition to chronic HCV disease. In these patients intolerance of antiretroviral therapy after OLT was associated with HIV disease progression. The two survivors show a stable liver function and non-progredient HIV infection under antiretroviral therapy 61 and 23 months after OLT, respectively.

Discussion: A medium- or even long-term survival after OLT can be achieved in HIV-infected patients without progression of HIV disease under antiretroviral therapy. However, in our study three out of five patients died due to graft failure. Therefore, prognostic criteria have to be defined for the selection of HIV-infected patients, who may benefit from OLT.

OP 8.1.
NF90ctv, a cellular dsRNA binding protein inhibits the Rev-dependent export of HIV-1 RNA

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Upon entering the uninfected host cell, the Human immunodeficiency virus type 1 (HIV-1) copies its single-stranded RNA genome into double-stranded DNA that is integrated into the host genome, at which step it is designated as provirus. The transcription of proviral DNA by host cell RNA polymerase II yields three types of viral transcripts: full spliced, singly spliced and unspliced transcripts. The spliced transcripts, are exported to the cytoplasm and translated as yielding the 'early' viral proteins, Tat, Rev and Nef. Among these, Rev possess the unique property of exporting unspliced and partially spliced viral transcripts that encode the structural viral proteins. The Rev-mediated nucleo-cytolasmic transport of viral RNA is strictly dependent upon its interaction with RRE RNA structural element present in the target molecules. Since the Rev-RRE complex formation depends on RNA-protein interactions, we reasoned that ectopic expression of a dsRNA-binding protein might interfere with normal Rev-mediated transposrt of RNAs that encode viral structural proteins. The double-stranded RNA (dsRNA) binding nuclear protein 90 (NF90) has been suggested to function as transcription activator of the IL-2 gene by binding to the ARRE-2 sequence present in the promoter region. We studied the properties of a C-terminal variant of NF90 (NF90ctv), in stably transduced HIV-1 target cell line (GHOST/CD4+/CXCR4+ cells), and observed marked attenuation of viral replication (krasnoselskya-Riz et al., 2002). The in vitro studies reported here suggest a mechanism of inhibition of Rev-function and viral replication that may include NF90ctv-mediated interference of HIV-1 Rev based on protein-protein interactions that involve Rev binding to specific domains of NF90ctv.

OP 8.2.
Expression of HIV-1 gp160 in Transgenic Animals.

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The human immunodeficiency virus (HIV-1) is known for its ability to primarily infect lymphocytes T CD4+ as well as monocytes/macrophages. Productive infection has also been reported in brain tissue, gut epithelium and bone marrow cells. The infection with HIV-1 leads to a progressive degeneration of the immune system and a neurological dysfunction, termed AIDS dementia complex.

AIDS has been related to the striking loss of CD4+ T cells. However, the mechanisms underlying the neurological disorder are still not well understood. Previous in vitro studies have shown that the viral glycoprotein gp120 is toxic for cells of neuronal origin, which suggested that this toxic effect could possibly account for the ADC frequently observed in patients at their late stage of disease. Hence, we have constructed recombinant plasmids with the gp160 gene under the control of different heterologous promoters. We assessed the expression in vitro first, to test for the ability of those promoters to drive the expression of HIV-1 gp120 and later used the constructs to develop our transgenic mice. We analyzed different organs of the transgenic animals for the expression of gp160, at the RNA and protein levels, and examined different tissues for eventual harms. The methodology and results will be discussed during the presentation.

OP 8.3.
Polymorphisms in CCR5 promoter are associated with rare HIV-1 infection of the D32/D32 homozygous individuals

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Human CC chemokine receptor 5 (CCR5) is the coreceptor for macrophage-tropic (R5) HIV-1 isolates. Individuals lacking this coreceptor are highly protected against HIV-1 infection. The CCR5 gene in these individuals has been found to contain a 32-bp deletion that results in a frame-shift mutation and produces a truncated protein that cannot function as a coreceptor. In a recent study, we demonstrated that expression of CCR5D32 protein downmodulates the HIV coreceptor expression resulting in protection against HIV-1 infection (Agrawal et al., Journal of Virology 78 (5): 2277). Although the D32/D32 homozygous genotype is associated with protection against infection, some rare individuals with this genotype have been found seropositive for HIV-1. The mechanisms of HIV-1 infection of these individuals are unknown. To explore possible mechanisms, we analyzed six different infected individuals with the D32/D32 homozygous genotype. Our results demonstrate that the CCR5D32 protein encoded by the deleted CCR5 gene was detectable in all uninfected D32/D32 individuals examined and only one infected homozygous individual. However, the levels of CCR5D32 protein in that infected individual were severely reduced compared to those in uninfected D32/D32 individuals. The CCR5D32 protein was not detectable in five different infected D32/D32 individuals. The reasons for the absence of detectable protein varied from polymorphisms in their CCR5 promoter region, different patterns of transcription, or a point mutation in CCR5D32 ORF in one individual that resulted in an unstable protein. The effect of promoter polymorphisms was directly examined in a reporter gene activation assay system. Quantitation of the mRNA produced endogenously in PBMCs of the infected individuals correlated well with weak CCR5 promoter activity in vitro using individuals promoter constructs driving firefly luciferase gene. These results demonstrate that expression of CCR5D32 protein is critical for protection against HIV-1 infection in vivo.

OP 8.4.
Evaluation of porcine thymic xenografts to restore human thymopoiesis that is resistant to HIV infection

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Highly active antiretroviral therapy (HAART) has dramatically changed the prognosis of human immunodeficiency virus (HIV) infection. However, immune reconstitution, a critical component of recovery after treatment of HIV-1 infection, is not always achieved following HAART. We have previously demonstrated that porcine thymic xenografts support human thymopoiesis in immune deficient mice, and that the human T cells that develop in these grafts are specifically tolerant to the porcine thymus donors. We hypothesized that porcine thymic xenografts might provide an HIV resistant milieu for human immune reconstitution in the setting of HIV-1 infection. Human fetal liver tissue was grafted with human or porcine thymic tissues (Hu/Hu and Sw/Hu grafts, respectively) under the kidney capsule of NOD/SCID recipient mice that received 1.5 Gy total body irradiation. The grafted animals also received an intravenous injection of 1x104 CD34+ cells isolated from human fetal liver tissue. Recipient mice were then followed for human T lymphocytes in their peripheral blood, and at 10 weeks post-transplantation, those with human T cell reconstitution either received an intragraft injection of 2000 TCID50 of NL4.3 HIV strain or were mock- infected with supernatant from uninfected control PBMC culture. Mice from various experimental groups were sacrificed at 3 weeks post-infection, and different tissues including blood and grafts were harvested. Plasma viral RNA load, the size of the grafts and expression of mouse CD45 (Ly-5), porcine CD2 (MSA-4), human (h)CD3, hCD4, hCD8, AnnexinV, HIV antigen p24 and BCL-2 were assessed using appropriate techniques. Our results showed that the cellularity of NL4.3-infected Sw/Hu grafts was in the same range as that of mock infected human and swine grafts. In contrast, there was a marked loss of cellularity in NL4.3-infected Hu/Hu grafts. There was a significant decrease in the numbers of CD3+, CD4 single positive (SP) and CD8SP human T cells in the periphery and of double positive (DP) and double negative (DN) as well as CD3+, CD4SP, CD8SP human T cells in the grafted tissues of NL4.3-infected compared to mock-infected Hu/Hu recipient mice. In contrast, these numbers remained similar between NL4.3-infected Sw/Hu and mock-infected Sw/Hu or Hu/Hu recipients. Expression of p24 and AnnexinV was also markedly higher in the NL4.3-infected Hu/Hu compared to Sw/Hu recipients infected with NL4.3. In contrast to the levels of p24 and AnnexinV, the expression of BCL-2 was suppressed in various subsets of human thymocytes, especially DP and CD4SP T cells of NL4.3-infected Hu/Hu recipients, while it displayed a normal pattern of expression in all other recipient groups. The level of plasma viral RNA was comparable in both NL4.3-infected Hu/Hu and Sw/Hu recipients. These data suggest that swine thymic xenografts may permit immune reconstitution in patients with resistant T-tropic HIV infections by protecting human thymocytes from HIV-mediated destruction.

OP 8.5.
Pol mutations and polymorphisms associated with NRTI and NNRTI-based regimens in Batswana patients infected with HIV-1 C.

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Background
HIV-1 subtype C (HIV-1C) is the predominant virus causing AIDS epidemic in Botswana, a country with an adult prevalence rate of HIV infection of approximately 35%. Nationwide introduction of HAART in Botswana in early 2002 necessitated characterization of pol polymorphisms and mutation patterns in the treated IV-1C infection.

Methods
Twenty-two patients attending the Infectious Disease Care Clinic (IDCC) of Princess Marina Hospital between May 2001 and March 2003 were included in this study. Among the sixteen ARV-treated patients, 8 started HAART regimens containing ddI/d4T/NVP or EFV (arm A) while the 8 others started the CBV/NVP or EFV regimen (arm B), the first line regimen currently provided by the Botswana ARV national program. Longitudinal samples were sequenced for the region encompassing the entire HIV-1 protease and the first 335 amino acids of reverse transcriptase. Translated amino acid sequences were analyzed for the presence of polymorphisms and mutations associated with drug resistance.

Results
Although polymorphisms were found in both naïve and treated patients, many of them (K20R, K22N, E40D, V60I, I135T, I142V, K166R, K281R) were primarily observed in treated patients. Primary mutations associated to NNRTI and NRTI resistance were only observed in 10 out of the 16 treated patients. The V106M mutation, previously shown as associated with EFV resistance in HIV-1 C, was harbored by a patient treated with NVP. Appearance of the M184V mutation in the arm B patients (CBV/NVP or EFV) coincided with a slight rebound of viral load (4.3±0.1 $\log_{10}$ RNA copies/ml) and significantly improved immunologic parameter (CD4=207.0±48.1 cells/µl; $p<0.05$). Interestingly, patients developing M184V mutation preferentially harbored polymorphisms Q174K and/or I178L located in the close proximity to the RT position 184. These patients also developed I135x polymorphism at the same time than M184V mutation.

Conclusion
The M184V mutation was associated with a clear clinical benefit at the time of its occurrence in 3TC-containing HAART. The co-existance of specific polymorphism in patients harboring M184V mutation associated with their localization in RT containing this primary mutation may warrant further studies including analysis of HIV-1C RT-specific T cell immune responses.

OP 8.6.
Aminoglycoside-arginine Conjugates: Chemical Barriers of HIV-1 entry

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We have designed and synthesized aminoglycoside arginine conjugates (AACs) as anti HIV-1 agents (1-3). The most potent anti-HIV-1 AAC is the hexa-arginine neomycin B conjugate (NeoR6). AACs inhibit HIV-1 replication, including the binding/fusion step of the viral cycle. Although designed as Tat antagonists, they also compete with monoclonal antibody binding to CXCR4, and with SDF-1 and HIV-1 gp120 cellular uptake, strengthening the notion that they interfere with initial steps of HIV-1 infection. Part of this competition may be explained by the structural mimicking of the AACs and gp120. The core and the number of arginines attached to a specific aminoglycoside are important for their anti-HIV potency (3). NeoR6 resistant isolates have the following mutations in the surface glycoprotein gp120: I249T in the C3 region, S283L in the V4 region, and Q306L in the C4 region; and in the transmembrane glycoprotein gp41: S640R and F645Y in the 'heptad repeat' 2 (HR2) (4). This strongly suggest that NeoR6 obstruct HIV-1 replication by interfering with the fusion step, dependant of both conformational changes in gp120 following CD4 and CXCR4 interaction, as well as by conformational changes in gp41 induced by HR1 and HR2 interaction. One mutation in the gp120 C4 region associated with a change of nonpolar (Q) to polar (K) amino acid residues. Similarly, two positions in the HR2 of gp41 are associated with changes of nonpolar (S and F) to polar (R and Y) amino acid residues. Nonpolar residues appear to be important for the antiviral activity of NeoR6. The role of the V3 domain in the interaction of gp120 with CXCR4 has not been directly demonstrated; variable domains such as V1/V2 and V3 of gp120 can both contribute to the interaction with CXCR4 coreceptor. Therefore, mutations in NeoR6 resistant isolates may confer resistance by allowing the interaction of gp120 with CXCR4 in such a way that NeoR6 interference would be minimized. The mechanism of the dual functions of NeoR6, inhibiting HIV-1 entry by binding CXCR4 coreceptor and inhibiting the fusion process is being further investigated. The AACs may thus represent a novel family of fusion inhibitors. References: 1. Litovchick et al, Biochemistry 39:2838, 2000. 2. Litovchick et al, Biochemistry 40: 15612, 2001. 3. Borkow et al, Antiviral Research 60:181, 2003. 4. Borkow et al, BBRC 312:1047, 2003.

OP 8.7.
Pharmacological Blockade Of Receptors Connecting To Inhibitory Pathways Of Immune Cells May Be An Efficient Immunopotentiating Treatment Of HIV/AIDS

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Introduction: HIV infection utilizes the inhibitory cAMP-PKA pathway of CD4 cells to enhance itw own replication and simultaneously to downregulate the performance of the CD4 cell by shutting it down via upregulation of the cAMP-PKA pathway. It has been shown for example that Methamphetamine feeding the cAMP-PKA pathway upregulates HIV-replication 15-fold, therefore drugs blocking receptors feeding this pathway may be very efficient in blocking not only the replication of HIV but at the same time would enhance the general performance of the CD4 cell and could be an interesting additional approach in the treatment of HIV/AIDS. Two examples of receptors connected to the cAMP-PKA pathway in cells of the immune system will be presented including clinical observations confirming an enhanced performance of the immune system with pharmacological blockade of this pathway.

Methods: Theoretical review.

Results: Pharmacological blockade of receptors feeding the cAMP-PKA pathway can be used as an HIV/AIDS treatment downregulating HIV-replication and enhancing the performance of the immune system, especially of CD4 cells.

OP 8.8.
Structure of Viral Antitermination Complexes

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The HIV Tat/TAR system is supposed to work as an antitermination system, similar to the better known antitermination systems from phages lambda and HK022. Antitermination is a necessary step in HIV replication, and disruption of the antitermination complex consisting of Tat protein, TAR recognition RNA, human cyclin T1, and RNA Polymerase II would prevent viral proliferation. No drug, however, that specifically and efficiently targets the HIV antitermination complex is known so far. In order to progress towards the rational, structure based construction of inhibitors of the formation of the HIV antitermination complex it would be highly desirable to obtain information on the three-dimensional structure of this complex. Although the tertiary structures of several peptid-RNA complexes involved in viral antitermination have been determined in recent years, the HIV antitermination complex itself has eluted all efforts to this end.
In addition to the HIV system, we study the bacteriophage lambda antitermination factor, N protein, and its RNA and protein complexes in a more general approach towards the understanding of the mechanisms involved in antitermination processes. N protein prevents termination of transcription by E. coli RNA polymerase at rho-dependent and independent terminators in the lambda early operons. The modifications of the RNA polymerase by the N protein requires the nutboxB hairpin of N utilization sites (nut) and the E. coli factors NusA, NusB, NusG, and NusE to form the stable and processive antitermination complex. As HIV Tat, N protein contains an arginine-rich RNA binding motif (ARM) at the NH2-terminus responsible for specific recognition of nutboxB-RNA (boxB). NMR and CD experiments indicate that free N protein is unstructured in solution and becomes partially structured only upon binding to boxB. The NH2 -terminal peptide N(1-36) is sufficient to ensure boxB binding, and all structural changes in N protein that occur upon binding to boxB are localized within this peptide. The COOH-terminal region is required for binding to NusA and the RNA polymerase. Nun protein from coliphage HK022 binds to boxB RNA as well but, in contrast to N protein, functions as a transcriptional terminator.
We expressed and isotopically labeled several proteins and protein domains of the antitermination complexes of HIV, phage lambda, and phage HK022 (e.g., N, Nun, RNA-Polymerase, NusA, Tat, cycT1) and, for the latter two system, could directly show by NMR-titrations that the interaction sites between the various proteins are highly modular, and their interaction domains are basically independent of the rest of the proteins. We were able to determine large parts of the structure of these antitermination complexes by NMR and molecular dynamics calculations.

OP 8.9.
The VirtualPhenotype™ Analysis of an HIV-1 Genotype Provides a More Accurate Prediction of Drug Susceptibility Than a Single Phenotype Measurement

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INTRODUCTION: VirtualPhenotype™ provides a quantitative prediction of antiretroviral drug resistance based on a database of viral genotypes and corresponding phenotypes for >32,000 clinical isolates. When a genotype is analyzed, drug-specific patterns of resistance-associated mutations are identified and isolates with similar patterns of mutations are selected from the database. The matching phenotypes of these isolates are averaged to provide a prediction of fold-change (FC) in IC_{50} relative to a reference wild-type. Here we assess the contribution of phenotype assay variability to observed differences between predicted and measured values.

METHODS: VirtualPhenotype™ analysis was performed on a panel of 7 clinical isolates with a broad range of drug-resistance levels. The panel was repeatedly tested over a period of two years for phenotype against 16 antiretroviral drugs, comprising a total of 733 measurements. The contribution of phenotype assay variability to observed differences between predicted and measured values was assessed by analysis of variance. FC, mean FC, and 95% confidence intervals were calculated for each drug for 1) individual phenotype test results, 2) the mean of replicate phenotype test results, and 3) VirtualPhenotype™ predictions.

RESULTS: The root mean square error (RMSE), an estimator of the standard deviation of the difference between measured and predicted phenotype, averaged 0.35 logFC (range: 0.27, lamivudine to 0.60, delavirdine). Phenotype assay variability was the major contributor to differences between measured and predicted FC values, accounting, on average, for 81% of RMSE. FC values predicted by VirtualPhenotype™ analysis corresponded very closely (r^2=0.93, $p<<0.0001$) to the mean of replicate phenotype measurements. For this panel of isolates, the number of matching geno-phenotypes available for predicting FC values ranged from 25 to 14318 (median = 325). Consequently, the confidence intervals for the predicted FC values were very small compared to those for individual or multiple replicate phenotype tests.

CONCLUSIONS: VirtualPhenotype™ analysis of HIV-1 genotype provides a precise, quantitative prediction of drug susceptibility phenotype. By averaging results across multiple isolates with similar mutational patterns, VirtualPhenotype™ overcomes the variability inherent in any biological assay and provides a prediction of drug susceptibility phenotype that is more precise than an individual phenotype measurement.

OP 9.1.
Chinese SARS and AIDS Control at Frontier Ports

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1. In last year, we have being taken Eight Measures and Five "None missed" fight SARS at frontier ports.
1.1 Eight Measures:
Health declaration;
Temperature check;
Medical tour of inspection;
Patient deportation;
Disinfection and ventilation;
Report Real-time epidemic information;
Self-protection;
Propaganda and education;

1.2 Five "None missed":
Fill in health declaration card without any one missed
Check temperature without any one missed .
Any one who has high fever (>38?)is sent to hospital without any one missed.
Every day report the SARS quarantine information without any one missed.
Every health declaration card is kept well without any one missed.

1.3 Effect of eight measures and Five "None missed" :
From April to July, 40.6 million entry-exit people had been checked by infrared temperature instrument;
33.5 million health declaration cards were checked;
15404 people were found to have some symptoms like SARS;
Five case were diagnosed as SARS;
No SARS case transmitted abroad through frontier ports;
No quarantine staff was infected by SARS;
2. From 1985 to 2003, 8.9million entry-exit people had been guarded past.1991 people with living HIV had been detected.

OP 9.2.
HIV-1 subtypes in the Northern Border Region of Kenya

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Background: Most molecular epidemiological studies of HIV in Kenya have been done in the central, western and coastal regions and areas bordering Uganda and Tanzania. In these regions, subtype A1 has been found to be dominant. No information exists about the situation of HIV-1 in northern Kenya, especially areas bordering Ethiopia, Sudan and Somalia. This study was carried out to determine the distribution of HIV-1 env subtypes along the northern Kenya border region.

Methods: One hundred and fifty two (152) HIV-1 antibody positive samples were collected from blood transfusion centres and STD clinics in Moyale, Kakuma, Mandera and Lokichogio. Proviral DNA was extracted and amplified using primers designed from a highly conserved region of group M and O sequences of gp41. Fragments of about 460bp spanning approximately 40 % of the gp41 region were amplified and sequenced directly. Sixty-two (62) of these samples were successfully analyzed and classified into HIV-1 subtypes by sequence-based phylogenetic analysis.

Results: Results of this analysis show that the following subtypes of HIV-1 are circulating in this region: Subtype C: 26 (42%); Subtype A1: 27 (43%) and Subtype D: 9 (15%).

Conclusions: Unlike other parts of Kenya where subtype A1 is dominant, the northern border region of Kenya has subtypes A1 and C in circulation in equal proportions.

OP 9.3.
Method of Treatment of Acquired Immune Deficiency Syndrome with Embryonic Hematopoietic Stem Cells

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This method is protected by two US patents: ? 5,811,089 from Sep. 22, 1998 and # US 6,184,033 B1 from Feb.6, 2001, Dutch patent # 194908 from Sep.15, 2003, and Russian patent #2137484 from Sep.20, 1999. It allows for stabilization and restoration of functional activity of the immune system and compensation of insufficient immune response of the patient with simultaneous decrease of clinical manifestations of the disease

The main group consisted of 48 patients for whom preliminary selection criteria have been developed: impossibility of antiviral therapy due to intolerance or considerable side effects; more than 50% decrease in CD4+ during preceding 6 months or reduction by 100/1 mm^3 during the same time; disease progression: transition from HIV to AIDS-AC, and from AIDS-AC into AIDS despite anti-virus therapy; impaired workability and quality of life (decrease in Karnofsky index by more than 20% during last 6 months); CD4+ count less than 50/mm3 with manifestations of AIDS-indicator diseases, and with Karnofsly index below 30%

Developed is an original cell composition containing embryonic hematopoietic stem cells. Its application led to increase of immune indices including CD4, CD3, CD8 subpopulations; the most demonstrative was this increase in the group of patients with CD4+ count 200-300 mm^3: at the end of the first post-transplant week, it rose by 35%, second week - by 72%, and in 1 and 6 months it was higher by respectively 51% and 42%. High levels of lymphocytes were maintained in patients in 3-6 and even in 10-12 months after transplantation. Reported were also normalization of peripheral blood count (leukocytes, erythrocytes, thrombocytes), decrease in infectious complications and manifestations of peripheral neuropathy and related neurological symptoms, disappearance of astheno-neurotic syndrome, optimization of psychoemotional state with decrease of depression signs, improvement of mental and physical activity, weight gain, and substantial inhibition of the progression of the disease.

OP 9.4.
Andrieu unjustly disregarded. Better CD4-counts with Prednisolone

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Background: In 1995 J.M. Andrieu (Paris) reported a CD4 increase with prednisolone in asymptomatic HIV patients. In the following years this was disregarded. Admittedly he used relatively high dosages, but the principle proved to be interesting: For a few years now we have noticed that the small dose of 5 mg Prednisolone, which can be used nearly without side effects for many years, has similar effects.

Methods: 60 therapy naïve patients with a CD4 count of at least 300/µl (mean 563) were treated for 0,5 - >11,5 years with prednisolone (5mg daily). CD4 profiles and viral load were compared retrospectively and ongoing with those of all untreated control patients (n = 133, mean CD4 612/µl). 128 patients received the same dosage of prednisolone >6 months during therapy interruptions (STI), 85 of them from the STI outset. They were compared with those receiving no prednisolone in their first 6 STI months (n = 41). Also the CD4-development of all patients with prednisolone during STI for >1 year, meanly 681 days, was documented (n = 99).

Results: A CD4 increase was observed in therapy naïve patients with prednisolone (after 3 years +127/µl), a decrease in the patients without prednisolone (after 3 years - 193/µl, p=0,0016). The same was observed in relative counts and CD4-/CD8-ratio. No significant difference, but also a trend in favour of prednisolone was determined in the development of the viral load. During STIs the CD4 decrease was more flat with prednisolone (0,46 instead of 0,77/die, p=0,0157). In 29 out of 39 (CD4) matched pairs the patients with prednisolone showed better CD4-development. Meanly all patients with prednisolone of the matched pairs lost 0,25 fewer CD4 cells/d. The mean CD4 count of the 99 STI patients taking prednisolone for >1 year sank from 672/µl to 524/µl. So STI could still be considerably increased in the majority.

Conclusions: It seems possible to reach a notable prolongation of time without HAART by means of low-dose glucocorticoid therapy. This could be of importance when considering costs and side-effects of HAART.

OP 9.5.
Enhanced Immunogenicity of HIV-1 Whole Killed Vaccine in Association with Amplivax™

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The immunogenicity of HIV-1 Immunogen combined with Amplivax™, a second-generation immunomodulatory oligonucleotide, was examined in two different model systems. HIV-1 Immunogen, also known as REMUNE®, is a gp120- depleted HIV-1 antigen emulsified in Incomplete Freund's Adjuvant (IFA). In the first model, C57/BL6 mice immunized subcutaneously with a combination of HIV-1 Immunogen and AmplivaxTM showed significantly enhanced HIV-specific production of p24 antibody, HIV-specific IFN-γ (both quantity and number of CD4 and CD8 T cells producing it), chemokines (RANTES, MIP-1α, MIP-1β), and IL-10 when compared to HIV-1 Immunogen or Amplivax™ alone. Importantly, the enhancements by Amplivax™ were still observed if HIV-1 antigen was not emulsified with IFA. In the second model, Amplivax™ was investigated ex-vivo for its ability to enhance HIV antigen stimulation of PBMC isolated from HIV+ patients treated with antiretroviral therapy (ART). Patients were either non-immunized, or previously immunized with HIV-1 Immunogen. Both patient groups had comparable CD4 counts, HIV plasma viremia, duration of infection, and ART. showed that AmplivaxTM induced stronger HIV-specific cell-mediated immune responses in patients vaccinated with HIV-1 Immunogen, as measured by total spots produced in the IFN-γ ELISPOT assay and a higher percentage of alpha defensin-producing cells. Both effects were most evident using 1 μg/ml of Amplivax™.
Preliminary data from an ongoing clinical trial in drug-naive HIV+ patients suggest that HIV-1 Immunogen also has a positive effect on generation of HIV-specific immune responses in this patient population. The potential enhancing effect of Amplivax™ will be tested later this year in these patients that will have Amplivax™ added to the HIV-1 Immunogen as part of the vaccine.

OP 9.6.
ESAT-6 and CFP-10 derived peptides for diagnosis of TB infection in severely immunocompromized HIV-infected individuals

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HIV infection is considered the strongest risk factor for the development of tuberculosis (TB). The tuberculin skin test (TST), using PPD, is largely utilized for both diagnosis and screening. However, the broad antigenic cross-reactivity of PPD with antigens derived from several mycobacterial species causes the poor specificity of TST. Moreover, up to 50% of TB patients coinfected with HIV have a negative TST. M tuberculosis infection evokes a strong cell-mediated immune response, and detection of specific T cells might be a means to detect infection. We selected and pooled 5 highly immuno-genic and largely HLA-DR-restricted peptides of 20 aa in length, 3 deri-ved from ESAT-6 and 2 from CFP-10, two secretory proteins highly specific of M tuberculosis, and used as antigens in an ELISPOT-IFN-γ assay and compared with the responses to PPD and BCG antigens. 27 HIV-infected, severely immunocompromized individuals, and 41 HIV negative subjects were enrolled and classified for TB infection following directions of the American Thoracic Society. 9 HIV+ and 20 HIV- subjects were classified as 3 or 4 (active or previous TB). The ELISPOT-IFN-γ assay resulted high specific (87.5%) and sensitive (93.1%) for detection of M tuberculosis infection. 3 out of 18 (16.7%) class 0 (TST neg), but HIV-infected individuals responded to peptides. Conversely, 2 out of 9 (22.2%) HIV+ patients with active TB, both TST neg, did not respond to peptides. One had an immune reconstitution syndrome cha-racterized by a very high spontaneous activation of their lymphocytes able to mask any response to antigens or peptides. Of note, all the HIV+ patients that responded to peptides also responded to BCG, and all that where neg to BCG were also neg to peptides, while 8 out of 18 BCG pos did not respond to pepti-des (previously vaccinated or infected with mycobacteria other than tuberculo-sis; MOTT). The mean number of spot forming cells x million PBMC in response to peptides was significantly higher in TB class 3-4 subjects vs class 0 (but significantly lower in HIV+ respect to HIV- subjects; p=0.022). While no significant differences were observed between HIV+ and HIV- TB class 0 individuals. In conclusion, the pool of peptides resulted to be very specific and sensitive for diagnosis of TB infection, and able to discriminate between BCG-vaccinated or MOTT-infected individuals and TB infected individuals. Moreover, the test allowed to recognize TB infected individuals also in some severely immunocompromized, HIV+ subjects otherwise recognizable.

OP 9.7.
Why the patient's perspective is critical in the management of lipodystrophy?

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Background: Lipodystrophy may greatly impairs quality of life (QoL). Nevertheless, the recognition of the scientific value of QoL and more broadly the patient's perspective in evaluating therapies is questioned. It may be useful to quantify the added value of the patient's perspective, using correlations between patient-reported outcomes (PROs) and clinician-reported and biological outcomes.

Methods: We performed a cross-sectional survey in 143 HIV French outpatients with lipodystrophy. Clinical and demographic data were collected. Patients completed a new specific lipodystrophy questionnaire "Assessment of Body Change and Distress" (ABCD), consisting of 3 parts: signs of lipodystrophy (6 items), global satisfaction (n=1) and 20 items evaluating QoL. A HIV specific (MOS-HIV) and generic (SF-12) QoL questionnaires were also filled-in.

Results: Mean age was 43 ± 10 yrs (71% of men), and mean duration of HAART was 4.5 ± 1.7 yrs. ABCD QoL score is weakly or no associated with viral load (r=0.03), CD4 count (r = 0.13) and CDC classification (p = NS). Its correlation with the clinician's report of number of sites of lipodystrophy is weak (r = 0.17). Correlations between different PROs are logically higher. ABCD QoL score is more correlated with the patient's report of number of sites of lipodystrophy (r = 0.39) and with satisfaction (r = 0.58). ABCD QoL score is correlated with health distress and social dimensions of the MOS-HIV (r > 0.6) and with mental component of the SF-12 (r = 0.65), but not with physical dimensions of these questionnaires (r < 0.2).

Conclusion: PROs are weakly correlated with biological markers, and although overlapping, each one of PROs measures a distinct concept. Clinicians cannot infer the QoL of their patients neither from a viral load nor from a clinical exam. The patient's perspective is essential in medical decision making and so it is with lipodystrophy.

OP 9.8.
A Technological Monitoring and Management-Support System for Anti-Retroviral Therapy in South Africa: Introducing Cell-Life

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The last ten years of democracy in South Africa have been characterised by developments to build a new nation. Basic amenities such as water, sanitation and electricity have been delivered to the majority of the population, and the housing backlog is being addressed. Developments are now being challenged through the impact of HIV/AIDS. Sub-Saharan Africa has an estimated 28.1 million HIV infections. Within this region, South Africa is faced with one of the most severe HIV/AIDS epidemics in the world, with estimates of infections ranging between 4 and 6 million. The South African Government's anti-retroviral (ARV) operational plan came into effect in November 2003, with early 2005 estimated for the ARV roll-out. The provision and distribution of medication is however a logistical problem, requiring a structure for correct delivery of treatment. South African research has shown that support of the HIV+ individual through home based care systems ensures a higher level of adherence. It has also been shown that accurate data about the individual, the medical history, the socio-economic status of the family and the individual's diet have a major impact on the success of adherence to ARV treatment. The collection of such data has until now been a major challenge. The non-governmental organisation (NGO) Cell-Life has developed a system that offers a 'bottom-up approach', whereby the home-based carer captures information via a user-friendly mobile phone (cellphone) application. South Africa has one of the highest uptakes and demographic distributions of cellular technology in the world. With this infrastructure and technology at hand, Cell-Life implemented an innovative information-gathering and provision system, which uses relatively simple and accessible, available technology to manage the treatment of HIV/AIDS in South Africa and the continent. Cellphone enabled Wireless Internet Gateway (WIG) applications which use Global System for Mobile Communications (GSM) networks, easy-to-use database applications on the Internet, an HIV/AIDS database, and a Geographical Information System (GIS) have resulted in an overall HIV/AIDS Information Management System. The system has been in use since August 2002 at pilot sites, and is presently being introduced in several trial ARV programmes. An independent study on the effectiveness of the system has shown that it improves the data recovery and treatment management over conventional systems; and with further enhancements it will form a solid foundation for the nationwide ARV rollout.

OP 10.1.
SARS: past, present, future

No abstract available